10-16-00

PATENT

Docket No. F-5076 DIV

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

NEW APPLICATION TRANSMITTAL
Under 37 CFR § 1.53(b)

Transmitted herewith for filing is the patent application of

Inventor(s): Robert Herman; John Chapman; Sun Chong-Son; Jean M. Mathias; Veronique Mayaudon; Serge deGheldere; Daniel Bischof

WARNING: *37 C.F.R. § 1.41(a)(1) points out:*

'(a) A patent is applied for in the name or names of the actual inventor or inventors.

(1) The inventorship of a nonprovisional application is that inventorship set forth in the oath or declaration as prescribed by § 1.63, except as provided for in § 1.53(d)(4) and § 1.63(c). If an oath or declaration as prescribed by § 1.63 is not filed during the pendency of a nonprovisional application, the inventorship is that inventorship set forth in the application papers filed pursuant to § 1. 53(b), unless a petition under this paragraph accompanied by the fee set forth in § 1.17(i) is filed supplying or changing the name or names of the inventor or inventors.

For (title): Systems and Methods for Removing Viral Agents from Blood

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CERTIFICATION UNDER 37 C.F.R. 1.10*
(Express Mail label number is mandatory.)
Express Mail certification is optional.)

I hereby certify that this New Application Transmittal and the documents referred to as attached therein are being deposited with the United States Postal Service on this date 13October 2000, in an envelope as 'Express Mail Post Office to Addressee' mailing Label Number EL574873804US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Judith Biebel
(type or print name of person mailing paper)

Judith D Biebel
Signature of person mailing paper

WARNING: *Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.*

WARNING: *Each paper or fee filed by "Express Mail" **must** have the number of the Express Mail mailing label placed thereon prior to mailing. 37 CFR 1.10(b).*
"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will not be granted on petition. 'Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

1. Type of Application

This new application is for a(n)

(check one applicable item below)

[ ] Original (nonprovisional)

[ ] Design

[ ] Plant

WARNING: ***Do not*** *use this transmittal for a completion in the U.S. of an International Application under 35 U.S.C. 371(c)(4), unless the International Application is being filed as a divisional, continuation or continuation-in-part application.*

WARNING: ***Do not*** *use this transmittal for the filing of a provisional application.*

NOTE: If one of the following 3 items apply then complete and attach ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF A PRIOR U.S. APPLICATION CLAIMED and a NOTIFICATION IN PARENT APPLICATION OF THE FILING OF THIS CONTINUATION APPLICATION.

[x] Divisional.

[ ] Continuation.

[ ] Continuation-in-part (C-I-P).

2. Benefit of Prior U.S. Application(s) (35 U.S.C. 119(e), 120, or 121)

NOTE: A nonprovisional application may claim an invention disclosed in one or more prior filed copending nonprovisional applications or copending international applications designating the United States of America. In order for a nonprovisional application to claim the benefit of a prior filed copending nonprovisional application or copending international application designating the United States of America, each prior application must name as an inventor at least one inventor named in the later filed nonprovisional application and disclose the named inventor's invention claimed in at least one claim of the later filed nonprovisional application in the manner provided by the first paragraph of 35 U.S. C. 112. Each prior application must also be:

(i) An international application entitled to a filing date in accordance with PCT Article 11 and designating the United States of America; or
(ii) Complete as set forth in § 1.51(b); or
(iii) Entitled to a filing date as set forth in § 1.53(b) or § 1.53(d) and include the basic filing fee set forth in § 1.16; or
(iv) Entitled to a filing date as set forth in § 1.53(b) and have paid therein the processing and retention fee set forth in § 1.21(l) within the time period set forth in § 1.53(f).
37 C.F.R. § 1.78(a)(1).

NOTE: If the new application being transmitted is a divisional, continuation or a continuation-in-part of a parent case, or where the parent case is an International Application which designated the U.S., or benefit of a prior provisional application is claimed, then check the following item and complete and attach ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

WARNING: If an application claims the benefit of the filing date of an earlier filed application under 35 U.S.C. 120, 121 or 365(c), the 20-year term of that application will be based upon the filing date of the earliest U.S. application that the application makes reference to under 35 U.S.C. 120, 121 or 365(c). (35 U.S.C. 154(a)(2) does not take into account, for the determination of the patent term, any application on which priority is claimed under 35 U.S.C. 119, 365(a) or 365(b).) For a c-i-p application, applicant should review whether any claim in the patent that will issue is supported by an earlier application and, if not, the applicant should consider canceling the reference to the earlier filed application. The term of a patent is not based on a claim-by-claim approach. See Notice of April 14, 1995, 60 Fed. Reg. 20,195, at 20,205.

WARNING: When the last day of pendency of a provisional application falls on a Saturday, Sunday, or Federal holiday within the District of Columbia, any nonprovisional application claiming benefit of the provisional application must be filed prior to the Saturday, Sunday, or Federal holiday within the District of Columbia. See 37 C.F.R. § 1.78(a)(3).

[x] The new application being transmitted claims the benefit of prior U.S. application(s). Enclosed are ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

3. Papers Enclosed

A. Required for filing date under 37 C.F.R. § 1.53(b) (Regular) or 37 C.F.R. § 1.153 Design) Application

25	Pages of specification
12	Pages of claims
01	Abstract
11	Sheets of drawing
[ ]	formal
[x]	informal

B. Other documents enclosed:

WARNING: DO NOT submit original drawings. A high quality copy of the drawings should be supplied when filing a patent application. The drawings that are submitted to the Office must be on strong, white, smooth, and non-shiny paper and meet the standards according to § 1.84. If corrections to the drawings are necessary, they should be made to the original drawing and a high-quality copy of the corrected original drawing then submitted to the Office. Only one copy is required or desired. For comments on proposed then-new 37 CFR 1.84, see Notice of March 9, 1988 (1990 O.G. 57-62).

NOTE: "Identifying indicia, if provided, should include the application number or the title of the invention, inventor's name, docket number (if any), and the name and telephone number of a person to call if the Office is unable to match the drawings to the proper application. This information should be placed on the back of each sheet of drawing a minimum distance of 1.5 cm. (518 inch) down from the top of the page . . ." 37 C.F.R. 1.84(c)).

(complete the following, if applicable)

[ ] The enclosed drawing(s) are photograph(s), and there is also attached a "PETITION TO ACCEPT PHOTOGRAPH(S) AS DRAWING(S)." 37 C.F.R. 1.84(b).

4. Additional papers enclosed

[x] Preliminary Amendment
[x] Information Disclosure Statement (37 C.F.R. 1.98)
[x] Form PTO-1449
[ ] Citations
[ ] Declaration of Biological Deposit
[ ] Submission of "Sequence Listing," computer readable copy and/or amendment pertaining thereto for biotechnology invention containing nucleotide and/or amino acid sequence.
[ ] Authorization of Attorney(s) to Accept and Follow Instructions from Representative
[ ] Special Comments
[ ] Other

5. Declaration or oath

NOTE: A newly executed declaration is not required in a continuation or divisional application provided that the prior nonprovisional application contained a declaration as required, the application being filed is by all or fewer than all the inventors named in the prior application, there is no new matter in the application being filed, and a copy of the executed declaration filed in the prior application (showing the signature or an indication thereon that it was signed is submitted. The copy must be accompanied by a statement requesting deletion of the names of person(s) who are not inventors of the application being filed. If the declaration in the prior application was filed under § 1.47, then a copy of that declaration must be filed accompanied by a copy of the decision granting § 1.47 status or if a nonsigning person under § 1.47 has subsequently joined in a prior application, then a copy of the subsequently executed declaration must be filed. See 37 C.F.R. ff 1.63(cO.

[x] Enclosed
- [ ] newly executed
- [x] copy from parent application identified above

Executed by *(check all applicable boxes)*
- [x] inventor(s).
- [ ] legal representative of inventor(s). 37 CFR 1.42 or 1.43.
- [ ] joint inventor or person showing a proprietary interest on behalf of inventor who refused to sign or cannot be reached.
  - [ ] This is the petition required by 37 CFR 1.47 and the statement required by 37 CFR 1.47 is also attached. See Item 13 below for fee.

[ ] Not Enclosed.

NOTE: Where the filing is a completion in the U.S. of an International Application or where the completion of the U.S. application contains subject matter in addition to the International Application, the application may be treated as a continuation or continuation-in-part, as the case may be, utilizing ADDED PAGE FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION CLAIMED.

[ ] Application is made by a person authorized under 37 C.F.R. 1.41(c) on behalf of all the above named inventor(s).
(The declaration or oath, along with the surcharge required by 37 CFR 1. 16(e) can be filed subsequently).

NOTE: It is important that all the correct inventor(s) are named for filing under 37 CFR 1.41(c) and 1.53(b).

[ ] Showing that the filing is authorized.
(not required unless called into question. 37 CFR 1.41(d))

6. Inventorship Statement

WARNING: If the named inventors are each not the inventors of all the claims an explanation, including the ownership of the various claims at the time the last claimed invention was made, should be submitted.

The inventorship for all the claims in this application are:

[x] The same.

or

[ ] Not the same. An explanation, including the ownership of the various claims at the time the last claimed invention was made

- [ ] is submitted.
- [ ] will be submitted.

7. Language

NOTE: An application including a signed oath or declaration may be filed in a language other than English. An English translation of the non-English language application and the processing fee of $130.00 required by 37 CFR 1.17(k) is required to be filed with the application, or within such time as may be set by the Office. 37 CFR 1.52(d).

[x] English
[ ] Non-English
  [ ] The attached translation includes a statement that the translation is accurate. 37 C.F.R. 1.52(d).

8. Assignment

[x] An assignment of the Invention to Baxter International Inc.
  [ ] is attached. A separate [ ] COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION or [ ] FORM PTO 1595 is also attached.
  [ ] will follow.
  [x] was filed in the parent application identified above

NOTE: "If an assignment is submitted with a new application, send two separate letters - one for the application and one for the assignment" Notice of May 4, 1990 (1114 O.G. 77-78).

WARNING: A newly executed "CERTIFICATE UNDER 37 CFR 3.73(b) must be filed when a continuation-in-part application is filed by an assignee. Notice of April 30, 1993, 11,50 O.G. 62-64.

9. CERTIFIED COPY

Certified copy(ies) of application(s)

Country	Appln. No.	Filed
Country	Appln. No.	Filed
Country	Appln. No.	Filed
Country	Appln. No.	Filed

from which priority is claimed

[ ] is (are) attached.

[ ] will follow.

NOTE: The foreign application forming the basis for the clam for priority must be referred to in the oath or declaration. 37 CFR 1.55(a) and 1.63.

NOTE: This item is for any foreign priority for which the application being filed directly relates. If any parent U.S. application or International Application from which this application claims benefit under 35 U.S.C. 120 is itself entitled to priority from a prior foreign application, then complete item 18 on the ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

10. **Fee Calculation** (37 C.F.R. 1.16)

A. [x] Regular application

CLAIMS AS FILED					
	Number Filed	Number Extra		Rate	Basic Fee 37 CFR 1.16(a) $710.00
Total Claims (37 CFR 1.16(c))	35	-20 = 15	x	$ 18.00	270.00
Independent Claims (37 CFR 1.16(b))	4	-3 = 1	x	$ 80.00	80.00
Multiple dependent claim(s) if any (37 CFR 1.16(d))			+	$270.00	270.00

[ ] Amendment canceling extra claims is enclosed.
[ ] Amendment deleting multiple-dependencies is enclosed.
[ ] Fee for extra claims is not being paid at this time.

NOTE: If the fees for extra claims are not paid on filing they must be paid or the claims cancelled by amendment, prior to the expiration of the time period set for response by the Patent and Trademark Office in any notice of fee deficiency. 37 CFR 1. 16(d).

Filing Fee Calculation 1330.00

B. [ ] Design application
($330.00 - 37 CFR 1.16(f))
Filing Fee Calculation _____

C. [ ] Plant application
($540.00 - 37 CFR 1.16(g))
Filing Fee Calculation _____

11. **Small Entity Statement(s)**

[ ] Statement(s) that this is a filing by a small entity under 37 CFR 1.9 and 1.27 is (are) attached.

WARNING: "Status as a small entity must be specifically established in each application or patent in which the status is available and desired. Status as a small entity in one application or patent does not affect any other application or patent, including applications or patents which are directly or indirectly dependent upon the application or patent in which the status has been established. The refiling of an application under § 1.53 as a continuation, division, or continuation-in-part (including a continued prosecution application under § 1.53(d)), or the filing of a reissue application requires new determination as to continued entitlement to small entity status for the continuing or reissue application. A nonprovisional application claiming benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) of a prior application, or a reissue application may rely on a statement filed in the prior application or in the patent if the nonprovisional application or the reissue application includes a reference to the statement in the prior application or in the patent or includes a copy of the statement in the prior application or in the patent and status as a small entity is still proper and desired. The payment of the small entity basic statutory filing fee will be treated as such a reference for purposes of this section." 37 C.F.R. § 1.28(a)(2).

(complete the following, if applicable)

[ ] Status as a small entity was claimed in prior application Serial No. ______________ filed on ____________________, from which benefit is being claimed for this application under 35 U.S.C., 119(e), 120, 121, or 365(c) and which status as a small entity is still proper and desired.

[ ] A copy of the statement in the prior application Is included.
Filing Fee Calculation (50% of A, B or C above)

$________________

NOTE: *Any excess of the full fee paid will be refunded if small entity status is established and a refund request are filed within 2 months of the date of timely payment of a full fee. The two-month period is not extendable under § 1.136, 37 CFR 1.28(a).*

12. Request for International-Type Search (37 C.F.R. 1.104(d))

(complete, if applicable)

[ ] Please prepare an international-type search report for this application at the time when national examination on the merits takes place.

13. Fee Payment Being Made at This Time

[ ] Not Enclosed

[ ] No filing fee is to be paid at this time.
(This and the surcharge required by 37 C.F.R. 1. 16(e) can be paid subsequently.)

[x] Enclosed

[x] Filing fee 1330.00

[ ] Recording assignment
($40.00; 37 C.F.R. 1.21(h))
(See attached 'COVER SHEET FOR ASSIGNMENT ACCOMPANYING NEW APPLICATION.) ________________

[ ] Petition fee for filing by other than all the inventors or person on behalf of the inventor where inventor refused to sign or cannot be reached
($130.00; 37 C.F.R. 1.47 and 1.17(i) ______________

[ ] For processing an application with a specification in a non-English language
($130.00; 37 C.F.R. 1.52(d) and 1.17(k)) ______________

[ ] Processing and retention fee
($130.00; 37 C.F.R. 1.53(d) and 1.21(l)) ______________

[ ] Fee for international-type search report
($40.00; 37 C.F.R. 1.21(e)) ______________

NOTE: *37 CFR 1.21(l) establishes a fee for processing and retaining any application that is abandoned for failing to complete the application pursuant to 37 CFR 1.53(o and this, as well as the changes to 37 CFR 1.53 and 1.78(a)(1), indicate that in order to obtain the benefit of a prior U.S. application, either the basic filing fee must be paid, or the processing and retention fee of § 1.21(l) must be paid, within 1 year from notification under § 53(f).*

Total fees enclosed 1330.00

14. Method of Payment of Fees

[x] Check in the amount of $ 1330.00 .

[ ] Charge Account No. ______________ in the amount of ______________.
A duplicate of this transmittal is attached.

NOTE: *Fees should be itemized in such a manner that it is clear for which purpose the fees are paid. 37 CFR 1.22(b).*

15. Authorization to Charge Additional Fees

WARNING *If no fees are to be paid on filing, the following items should not be completed.*
WARNING *Accurately count claims, especially multiple dependent claims, to avoid unexpected high charges, if extra claim charges are authorized.*

[x] The Commissioner is hereby authorized to charge the following additional fees by this paper and during the entire pendency of this application to Account No. 06-2360
- [x] 37 C.F.R. 1.16(a), (f) or (g) (filing fees)
- [x] 37 C.F.R. 1.16(b), (c) and (d) (presentation of extra claims)

NOTE: *Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 CFR 1.16(d)), It might be best not to authorize the PTO to charge additional claim fees, except possibly when dealing with amendments after final action.*
- [x] 37 C.F.R. 1.16(e) (surcharge for filing the basic filing fee and/or declaration on a date later than the filing date of the application)
- [x] 37 C.F.R. §§ 1.17(a)(l-5) (extension fees pursuant to § 1.136(a)).
- [x] 37 C.F.R. 1.17 (application processing fees)

NOTE: A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission. 37 C.F.R. 1. 136(a)(3).

[ ] 37 C.F.R. 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 CFR 1.311(b).

NOTE: 37 CFR 1.28(b) requires "Notification of any change in status resulting in loss of entitlement to small entity status must be filed in the application..... prior to paying, or at the time of paying, . . . issue fee." From the wording of 37 CFR 1.28(b), (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

16. Instructions as to Overpayment

NOTE ". . . Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account.' 37 C.F.R. § 1.26(a).

[x] Credit Account No. 06-2360

[ ] Refund

SIGNATURE OF PRACTITIONER

Reg. No. 29,243

Tel. No.: (262) 783 - 1300

Daniel D. Ryan
(type or print name of attorney)
RYAN KROMHOLZ & MANION, S.C.
(P.O. Address)
Post Office Box 26618

MILWAUKEE, WISCONSIN 53226

[x] Incorporation by reference of added pages

(check the following item if the application in this transmittal claims the benefit of prior U.S. application(s) (including an international application entering the U.S. stage as a continuation, divisional or C-I-P application) and complete and attach the ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED)

[x] Plus Added Pages for New Application Transmittal Where Benefit of Prior U.S. Application(s) Claimed

Number of pages added ______________

[ ] Plus Added Pages for Papers Referred to in Item 4 Above

Number of pages added ______________

[ ] Plus added pages deleting names of inventor(s) named in prior application(s) who is/are no longer inventor(s) of the subject matter claimed in this application.

Number of pages added ______________

[ ] "Assignment Cover Letter Accompanying New Application"

Number of pages added ______________

[ ] Statement Where No Further Pages Added

(if no further pages form a part of this Transmittal, then end this Transmittal with this page and check the following item)

[ ] This transmittal ends with this page.

ADDED PAGES FOR APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED

NOTE: "In order for an application to claim the benefit of a prior filed copending national application, the prior application must name as an inventor at least one inventor named in the later filed application and disclose the named inventor's invention claimed in at least one claim of the later filed application in the manner provided by the first paragraph of 35 U.S.C. 112." 37 CFR 1.78(a).

NOTE: "N ADDITION THE PRIOR APPLICATION MUST BE (1) COMPLETE AS SET FORTH IN S 1.51, OR (2) ENTITLED TO A FILING DATE AS SET FORTH IN S 1.53(B) AND INCLUDE THE BASIC FILING FEE SET FORTH IN S 1.16; OR (3) ENTITLED TO A FILING DATE AS SET FORTH IN S 1.53(B) AND HAVE PAID THEREIN THE PROCESSING AND RETENTION FEE SET FORTH IN S 1.21(L) WITHIN THE TIME PERIOD SET FORTH IN S 1.53(D)."37 CFR 1.78(A).

17. Relate Back-35 U.S.C. 120

NOTE: "NY APPLICATION CLAIMING THE BENEFIT OF A PRIOR FILED COPENDING NATIONAL OR INTERNATIONAL APPLICATION MUST CONTAIN OR BE AMENDED TO CONTAIN IN THE FIRST SENTENCE OF THE SPECIFICATION FOLLOWING THE TITLE A REFERENCE TO SUCH PRIOR APPLICATION IDENTIFYING IT BY SERIAL NUMBER AND FILING DATE OR INTERNATIONAL APPLICATION NUMBER AND INTERNATIONAL FILING DATE AND INDICATING THE RELATIONSHIP OF THE APPLICATIONS." 37 CFR 1.78(A). SEE ALSO THE NOTICE OF APRIL 28, 1987 (1079 O.G. 32 TO 46).

[x] Amend the specification by inserting the following information before the first line:

Related Application:
This application is a division of co-pending application Serial No. 08/742,572 filed October 28, 1996.

NOTE: THE PROPER REFERENCE TO A PRIOR FILED PCT APPLICATION WHICH ENTERED THE U.S. NATIONAL PHASE IS THE U.S. SERIAL NUMBER AND THE FILING DATE OF THE PCT APPLICATION WHICH DESIGNATED THE U.S.

NOTE: (1) WHERE THE APPLICATION BEING TRANSMITTED ADDS SUBJECT MATTER TO THE INTERNATIONAL APPLICATION THEN THE FILING CAN BE AS A CONTINUATION-IN-PART OR (2) IT IS DESIRED TO DO SO FOR OTHER REASONS, E.G. WHERE NO DECLARATION IS AVAILABLE, NO ENGLISH TRANSLATION IS AVAILABLE OR NO FEE IS TO BE PAID ON FILING THEN THE FILING CAN BE AS A CONTINUATION. IN THESE CASES THE INTERNATIONAL APPLICATION DESIGNATING THE U.S. IS TREATED AS THE PARENT CASE IN THE U.S. AND IS AN ALTERNATIVE TO THE COMPLETION OF THE INTERNATIONAL APPLICATION UNDER 35 U.S.C. 371(C)(4) WHICH MUST MEET THE REQUIREMENTS OF 37 CFR 1.61(A). THIS ALTERNATIVE PERMITS THE COMPLETION OF THE FILING REQUIREMENTS WITHIN ANY TERM SET BY THE PTO UNDER 37 CFR 1.53(D) TO WHICH THE EXTENSION PROVISIONS OF 37 CFR 1.136(A) APPLY. (WHEREAS, IF THE FILING IS AS AN INTERNATIONAL APPLICATION ENTERING THE U.S. STAGE THEN THE FEE, DECLARATION AND/OR ENGLISH TRANSLATION (WHERE NECESSARY) IS DUE WITHIN 20 MONTHS OF THE PRIORITY DATE BUT CAN BE PAID WITHIN 22 MONTHS OF THE PRIORITY DATE (OR IS DUE WITHIN 30 MONTHS OF THE PRIORITY DATE BUT CAN BE SUBMITTED WITHIN 32 MONTHS OF THE PRIORITY DATE) WITH THE SURCHARGES SET FORTH IN 37 CFR 1.492(E), (F) AND 37 CFR 1.495(C); HOWEVER, THE PROVISIONS OF 37 CFR 1.136 DO NOT APPLY TO THIS 22 OR (32 MONTH) PERIOD. 37 CFR 1.61(B).)

NOTE: THE DEADLINE FOR ENTERING THE NATIONAL PHASE IN THE U.S. FOR AN INTERNATIONAL APPLICATION WAS CLARIFIED IN THE NOTICE OF APRIL 28, 1987 (1079 O.G. 32 TO 46) AS FOLLOWS:

"The Patent and Trademark Office considers the International application to be pending until the 22nd month from the priority date if the United States has been designated and no Demand for International Preliminary Examination has been filed prior to the expiration of the 19th month from the priority date and until the 32nd month from the priority date if a Demand for International Preliminary Examination which elected the United States of America has been filed prior to the expiration of the 19th month from the priority date, provided that a copy of the international application has been communicated to the Patent and Trademark Office within the 20 or 30 month period respectively. If a copy of the international application has not been communicated to the Patent and Trademark Office within the 20 or 30 month period respectively, the international application becomes abandoned as to the United States 20 or 30 months from the priority date respectivley. These periods have been placed in the rules as paragraph (h) of S 1.494 and paragraph (i) of S 1.495. A continuing application under 35 U.S.C. 365(c) and 120 may be filed anytime during the pendency of the international application."

18. Relate Back-35 U.S.C. 119 Priority Claim for Prior Application

The prior U.S. application(s), including any prior International Application designating the U.S., identified above in item 17, in turn itself claim(s) foreign priority (ies) as follows:

country	appl. no.	filed on

The certified copy (ies) has (have)

[ ] been filed on _____ in prior application 0 /_____ which was filed on _____.

[ ] is (are) attached

WARNING: THE CERTIFIED COPY OF THE PRIORITY APPLICATION WHICH MAY HAVE BEEN COMMUNICATED TO THE PTO BY THE INTERNATIONAL BUREAU MAY NOT BE RELIED ON WITHOUT ANY NEED TO FILE A CERTIFIED COPY OF THE PRIORITY APPLICATION IN THE CONTINUING APPLICATION. THIS IS SO BECAUSE THE CERTIFIED COPY OF THE PRIORITY APPLICATION COMMUNICATED BY THE INTERNATIONAL BUREAU IS PLACED IN A FOLDER AND IS NOT ASSIGNED A U.S. SERIAL NUMBER UNLESS THE NATIONAL STAGE IS ENTERED. SUCH FOLDERS ARE DISPOSED OF IF THE NATIONAL STAGE IS NOT ENTERED. THEREFORE SUCH CERTIFIED COPIES MAY NOT BE AVAILABLE IF NEEDED LATER IN THE PROSECUTION OF A CONTINUING APPLICATION. AN ALTERNATIVE WOULD BE TO PHYSICALLY REMOVE THE PRIORITY DOCUMENTS FROM THE FOLDERS AND TRANSFER THEM TO THE CONTINUING APPLICATION. THE RESOURCES REQUIRED TO REQUEST TRANSFER, RETRIEVE THE FOLDERS, MAKE SUITABLE RECORD NOTATIONS, TRANSFER THE CERTIFIED COPIES, ENTER AND MAKE A RECORD OF SUCH COPIES IN THE CONTINUING APPLICATION ARE SUBSTANTIAL. ACCORDINGLY, THE PRIORITY DOCUMENTS IN FOLDERS OF INTERNATIONAL APPLICATIONS WHICH HAVE NOT ENTERED THE NATIONAL STAGE MAY NOT BE RELIED ON. NOTICE OF APRIL 28, 1987 (1079 O.G. 32 TO 46).

19. Maintenance of Copendency of Prior Application

NOTE: THE PTO FINDS IT USEFUL IF A COPY OF THE PETITION FILED IN THE PRIOR APPLICATION EXTENDING THE TERM FOR RESPONSE IS FILED WITH THE PAPERS CONSTITUTING THE FILING OF THE CONTINUATION APPLICATION. NOTICE OF NOVEMBER 5, 1985 (1060 O.G. 27).

A. [ ] Extension of time in prior application

(This item MUST BE COMPLETED AND THE PAPERS FILED IN THE PRIOR APPLICATION IF THE PERIOD SET IN THE PRIOR APPLICATION HAS RUN)

[ ] A petition, fee and response extends the term in the pending prior application until _____.

[ ] A copy of the petition filed in prior application is attached

B. [ ] Conditional Petition for Extension of Time in Prior Application

(complete this item if previous item not applicable)

[ ] A conditional petition for extension of time is being filed in the pending prior application.

[ ] A copy of the conditional petition filed in the prior application is attached

20. Further Inventorship Statement Where Benefit of Prior Application(s) Claimed

NOTE: *IF THE CONTINUATION, CONTINUATION-IN-PART, OR DIVISIONAL APPLICATION IS FILED BY LESS THAN ALL THE INVENTORS NAMED IN THE PRIOR APPLICATION A STATEMENT MUST ACCOMPANY THE APPLICATION WHEN FILED REQUESTING DELETION OF THE NAMES OF THE PERSON OR PERSONS WHO ARE NOT INVENTORS OF THE INVENTION BEING CLAIMED IN THE CONTINUATION, CONTINUATION-IN-PART, OR DIVISIONAL APPLICATION. 37 CFR 1.62(A) [EMPHASIS ADDED]. (DEALING WITH THE FILE WRAPPER CONTINUATION SITUATION).*

NOTE: *IN THE CASE OF A CONTINUATION-IN-PART APPLICATION WHICH ADDS AND CLAIMS ADDITIONAL DISCLOSURE BY AMENDMENT, AN OATH OR DECLARATION AS REQUIRED BY S 1.63 MUST BE FILED. IN THOSE SITUATIONS WHERE A NEW OATH OR DECLARATION IS REQUIRED DUE TO ADDITIONAL SUBJECT MATTER BEING CLAIMED, ADDITIONAL INVENTORS MAY BE NAMED IN THE CONTINUING APPLICATION. IN A CONTINUATION OR DIVISIONAL APPLICATION WHICH DISCLOSES AND CLAIMS ONLY SUBJECT MATTER DISCLOSED IN A PRIOR APPLICATION, NO ADDITIONAL OATH OR DECLARATION IS REQUIRED AND THE APPLICATION MUST NAME AS INVENTORS THE SAME OR LESS THAN ALL THE INVENTORS IN THE PRIOR APPLICATION. 37 CFR 1.60(C). (DEALING WITH THE CONTINUATION SITUATION).*

(complete applicable item (a), (b) and/or (c) below)

(a) [x] This application discloses and claims only subject matter disclosed in the prior application whose particulars are set out above and the inventor(s) in this application are

[x] the same.
[ ] less than those named in the prior application and it is requested that the following inventor(s) identified for the prior application be deleted:

____
(type name(s) of inventor(s) to be deleted)

(b) [ ] This application discloses and claims additional disclosure and a new declaration or oath is being filed. With respect to the prior application the inventor(s) in this application are

[ ] the same.
[ ] the following additional inventor(s) have been added

____
(type name(s) of inventor(s) to be added)

(c) The inventorship for all the claims in this application are

[x] the same.
[ ] not the same, and an explanation, including the ownership of the various claims at the time the last claimed invention was made

[ ] is submitted.
[ ] will be submitted.

21. Abandonment of Prior Application (if applicable)

[ ] Please abandon the prior application at a time while the prior application is pending or when the petition for extension of time or to revive in that application is granted and when this application is granted a filing date so as to make this application copending with said prior application.

NOTE: *ACCORDING TO THE NOTICE OF MAY 13, 1983 (103, TMOG 6-7) THE FILING OF A CONTINUATION OR CONTINUATION-IN-PART APPLICATION IS A PROPER RESPONSE WITH RESPECT TO A PETITION FOR EXTENSION OF TIME OR A PETITION TO REVIVE AND SHOULD INCLUDE THE EXPRESS ABANDONMENT OF THE PRIOR APPLICATION CONDITIONED UPON THE GRANTING OF THE PETITION AND THE GRANTING OF A FILING DATE TO THE CONTINUING APPLICATION.*

22. Petition for Suspension of Prosecution for the Time Necessary to File an Amendment

WARNING: *THE CLAIMS OF A NEW APPLICATION MAY BE FINALLY REJECTED IN THE FIRST OFFICE ACTION IN THOSE SITUATIONS WHERE (1) THE NEW APPLICATION IS A CONTINUING APPLICATION OF, OR A SUBSTITUTE FOR, AN EARLIER APPLICATION, AND (2) ALL THE CLAIMS OF THE NEW APPLICATION (A) ARE DRAWN TO THE SAME INVENTION CLAIMED IN THE EARLIER APPLICATION, AND (B) WOULD HAVE BEEN PROPERLY FINALLY REJECTED ON THE GROUNDS OF ART OF RECORD IN THE NEXT OFFICE ACTION IF THEY HAD BEEN ENTERED IN THE EARLIER APPLICATION." MPEP, S 706.07(B).*

NOTE: *WHERE IT IS POSSIBLE THAT THE CLAIMS ON FILE WILL GIVE RISE TO A FIRST ACTION FINAL FOR THIS CONTINUATION APPLICATION AND FOR SOME REASON AN AMENDMENT CANNOT BE FILED PROMPTLY (E.G., EXPERIMENTAL DATA IS BEING GATHERED) IT MAY BE DESIRABLE TO FILE A PETITION FOR SUSPENSION OF PROSECUTION FOR THE TIME NECESSARY.*

(check the next item, if applicable)

[ ] There is provided herewith a Petition To Suspend Prosecution for the Time Necessary to File An Amendment (New Application Filed Concurrently)

Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Divisional Application of

PARENT

Application of	:	Herman et al.	Examiner: P. Ponnaluri
Serial No.	:	08/742,572	Group Art Unit: 1648
Filed	:	October 28, 1996	
For	:	Systems and Methods for Removing Viral Agents from Blood	

PRELIMINARY AMENDMENT

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Please amend this divisional application prior to the first office action as follows:

IN THE DRAWINGS:

In Figs. 7, 8A, 8B, 9, 12A, and 12B, please change reference numeral "360" to --- 340 --- as indicated in red in the attached marked-up drawings.

In Fig. 9, please change reference numeral "306" to --- 302 --- as indicated in red in the attached marked-up drawings.

IN THE SPECIFICATION:

On page 15, line 15, please change "328" to --- 330 ---.

On page 16, line 27, please change "360" to --- 340 ---.

On page 18, line 26, please change "306" to --- 302 ---.

Please delete the sentence beginning on page 18, line 33, and ending on page 19, line 2, and insert in its place --- Further details of a light chamber can be found in Wolf et al. U.S. Patent 5,290,221 and Bischof et al. U.S. Patent 5,300,019. ---

IN THE CLAIMS:

Cancel claims 1-37; and 63 to 69.

Please consider the following new claims 70 to 76:

70 (New). A kit according to claim 42 further including

a first filtration media coupled to the tubing to separate a first cellular blood species from the blood constituent conveyed from the blood constituent source, and

a second filtration media coupled to the tubing in series with the first filtration media to separate a second cellular blood species from the blood constituent conveyed from the blood constituent source, to thereby produce a filtered blood constituent that is essentially free of the first and second cellular blood species.

71 (New). A kit according to claim 44

wherein the photoactive material includes psoralen.

72 (New). A kit according to claim 71

wherein the light filtering material includes a red material.

73 (New). A kit according to claim 49

wherein the photoactive material includes psoralen.

74 (New). A kit according to claim 73

wherein the light filtering material includes a red material.

75 (New). A kit according to claim 55

wherein the photoactive material includes psoralen.

76 (New). A kit according to claim 75

wherein the light filtering material includes a red material.

REMARKS

The Drawings and Specification have been amended in the same manner as the parent application. New claims 70 to 76 have been added. The forms that accompanied this application when filed further instructed the Office to cancel claims 1 to 37 and 63 to 69.

Claims 38 to 62 and 70 to 76 are pending in the application.

The Examiner's attention is directed to the Information Disclosure Statement that accompanies this divisional application. The Statement lists the documents that are of record in

the parent case Serial No. 08/742,572, filed October 28, 1996, and examined by Examiner Ponnaluri (Art Unit 1618).

Respectfully submitted,

By_____
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Registration No. 29,243

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SYSTEMS AND METHODS FOR REMOVING VIRAL AGENTS FROM BLOOD

Field of the Invention

The invention generally relates to the eradication of contaminants using photodynamic therapy. The invention also generally relates to the processing of whole blood and its components for storage and transfusion. In a more specific sense, the invention relates to the extracorporeal treatment of collected whole blood and its components with photoactive materials to eradicate viruses and other pathogenic contaminants.

Background of the Invention

With the coming of blood component therapy, most whole blood collected today is separated into its clinically proven components for storage and administration. The clinically proven components of whole blood include red blood cells, used to treat chronic anemia; platelet-poor plasma, from which Clotting Factor VIII-rich cryoprecipitate can be obtained for the treatment of hemophilia; and concentrations of platelets, used to control thrombocytopenic bleeding.

It is well known that blood can carry infectious agents like hepatitis-B virus; the human immunodeficiency (AIDS) virus; the Herpes virus; and the influenza virus. To avoid the transmission of these infectious agents during blood transfusions, donors of blood are routinely screened and also undergo serologic testing to detect the presence of these agents. Still, it is difficult to always assure that these

infectious agents are detected.

The use of photodynamic therapy has been suggested as a way to eradicate infectious agents from collected blood and its components. Still, there has been a general lack of success in economically adapting the benefits of photodynamic therapy to the demands of the blood banking industry. One reason for this is that not all biological contaminants are carried free within the blood where they can be readily coupled to photoactive agents. Some biological contaminants are entrained on or within white blood cells out of the reach of photoactive agents.

For this and other reasons, the promise of photodynamic therapy in treating the nation's banked blood supply has gone largely unfulfilled.

Summary of the Invention

The invention provides improved systems and methods for treating blood constituents to adventitious viral agents.

One aspect of the invention provides systems and methods which remove viral agents from plasma. The systems and methods remove from the plasma targeted cellular matter that does or might entrain viral agents. In a preferred embodiment, the targeted cellular matter includes leukocytes. The system and methods add to the plasma a photoactive material, which binds to viral agents that are free of entrainment by the targeted cellular matter. Radiation emitted at a selected wavelength into the plasma activates the photoactive material and thereby eradicates the free viral agents.

In a preferred embodiment, a system for treating plasma comprises tubing adapted to be coupled a plasma source, and a filter in the tubing to

separate cellular matter from the plasma conveyed from the source. The system includes a transfer container coupled to the tubing to receive cellular matter-reduced plasma from the filter, and a source of photoactive material to be mixed with the plasma. In this embodiment, the tubing includes a path to vent air from the transfer container in a path that bypasses the filter.

In a preferred embodiment, systems and methods remove viral agents entrained within the cellular matter by conveying plasma in a first path through a filter. The systems and methods convey the cellular matter-reduced plasma from the filter in a second path, which includes a connected transfer container. The systems and methods mix the cellular matter-reduced plasma with a photoactive material within the transfer container, forming a plasma mixture.

In this embodiment, the systems and methods convey a portion of the plasma mixture from the transfer container in a flush path, which includes the second path, to thereby expose residual contaminants in the second path to the photoactive material. The systems and methods then separate the transfer container from the filter by severing the second path. After severance from the filter, a remnant of the second path remains attached to the transfer container. However, due to the prior flushing step, all contaminants in the attached second path remnant have been exposed to the photoactive material. Subsequent radiation of the transfer container thereby eradicates contaminants, which are free of entrainment by cellular matter, both within the transfer container and the attached second path remnant.

In a preferred embodiment, the flush path by

passes the filter and also provides a path to vent air from the transfer container.

Another aspect of the invention provides systems and methods for treating plasma using multi-stage filtration, which targets for removal different species of cellular matter. The systems and methods separate a first species of cellular matter by filtration through a first filter media, thereby removing contaminants entrained within the first species of cellular matter. The systems and methods separating a second species of cellular matter by filtration through a second filter media, thereby removing contaminants entrained within the second species of cellular matter. The systems and methods add to the plasma a photoactive material and emit radiation at a selected wavelength into the plasma to activate the photoactive material, thereby eradicating the contaminant that is free of entrainment by cellular matter. In a preferred embodiment, the first filtration media targets leukocytes for removal, while the second filtration media targets platelets for removal.

Another aspect of the invention provides a kit that envelopes photoactive material in an overwrap that includes a light filtering material. The light filtering material absorbs light that activates the photoactive material. The presence of the light filtering material in the overwrap protects the photoactive material from photo-degradation due to absorption of ambient light during handling and storage prior to use.

In a preferred embodiment, the photoactive material within the kit includes methylene blue. In this embodiment, the light filtering material includes a blue material having phtalocyanine pigments.

In a preferred embodiment, the photoactive material is contained in liquid form within the kit. In this embodiment, the overwrap also includes material that reduces liquid vapor loss from the kit.

Other features and advantages of the invention will be pointed out in, or will be apparent from, the drawings, specification and claims that follow.

Description of the Drawings

Fig. 1 is a plane view of a blood processing and storage kit for reducing the presence of viral agents in plasma;

Fig. 2 is an exploded, perspective view of the laminated walls of the overwrap envelope shown in phantom lines in Fig. 1;

Fig. 3 is a side view of the laminated walls of the overwrap envelope shown in Fig. 2;

Fig. 4 is a top perspective view of the laminated walls of the overwrap envelope, after having been joined by a peripheral heat seal;

Fig. 5 is an exploded side view of the leukocyte reduction filter that forms a part of the kit shown in Fig. 1;

Fig. 6 is a top perspective view of the interior of the outlet housing part for the filter shown in Fig. 5;

Fig. 7 is a plane view the kit shown in Fig. 1 being used to convey plasma from a source container, through the leukocyte reduction filter, and into the processing and storage container;

Fig. 8A is a plane view the kit shown in Fig. 7 being used to vent air and residual plasma from the processing and storage container in a bypass path around the leukocyte reduction filter;

Fig. 8B is a plane view of the kit shown in Fig. 8A being used to flush the tubing section next to

the container with photoactive material, to assure exposure of residual viruses occupying the tubing section with photoactive material;

Fig. 9 is a perspective view of the kit shown in Figs. 8A and 8B, after separation of the processing and storage container and placement of the processing and storage container in an irradiation chamber;

Fig. 10 is a plane view of an alternative embodiment of a blood processing and storage kit for reducing the presence of viral agents in plasma, in which the photoactive material is stored within an auxiliary container whose walls include a light filtering material;

Fig. 11 is a plane view of an alternative embodiment of a blood processing and storage kit for reducing the presence of viral agents in plasma, which includes an integrally attached air reservoir;

Fig. 12A is a plane view of the kit shown in Fig. 11 being use to vent air and residual plasma from the processing and storage container into the air reservoir;

Fig. 12B is a plane view of the kit shown in Fig. 12A being used to flush the tubing section next to the container with photoactive material, to assure exposure of residual viruses occupying the tubing section with photoactive material; and

Fig. 13 is a plane view of another alternative embodiment of a blood processing and storage kit for reducing the presence of viral agents in plasma, which reduces the presence of viral agents in plasma by the removal by filtration of least two different cellular blood species which actually do or potentially can entrain viral agents.

The invention is not limited to the details

of the construction and the arrangements of parts set forth in the following description or shown in the drawings. The invention can be practiced in other embodiments and in various other ways. The terminology and phrases are used for description and should not be regarded as limiting.

Description of the Preferred Embodiments

Fig. 1 shows a blood constituent processing and storage set or kit 300. The kit 300 is intended, during use, to assist in the removal of viral agents from plasma. The viral agents are either carried free within the plasma or are entrained on or within cellular matter (e.g., red blood cells, platelets, and leukocytes) that the plasma carries. The kit 300 shown in Fig. 1 will be described in the context of reducing the presence of viral agents in single donor units of plasma, because it is particularly well suited for this purpose.

The kit 300 includes a processing and storage container 302, which carries an integrally attached length of flexible transfer tubing 304. In the illustrated embodiment, the transfer tubing 304 is made from medical grade plasticized polyvinyl chloride plastic. However, other flexible medical grade plastic materials can be used.

The transfer tubing 304 includes an integrally attached in-line filter 306. The filter 306 includes a filter media 307 (see Fig. 5) that removes from plasma cellular matter that does actually or potentially entrain viral agents.

As Fig. 5 shows, the filter media 307 is encased within a two part housing 348A and 348 B made, for example, from polycarbonate, although any engineering medical grade plastic with appropriate toxicology characteristics can be used. The housing

348A/348B is sealed about the filter media 307 by, for example, sonic welding.

The pore size of the filter media 307 can be tailored to remove by exclusion all or some species of cellular matter found in plasma, depending upon the extent to which viral agents sought to be eliminated are entrained by the different cellular species. In the illustrated embodiment, the principal cellular species targets of the filter 306 are leukocytes, for it is known that leukocytes entrain many viral agents. With this objective in mind, the filter media 307 comprises a non-fibrous membrane having a pore size smaller than the size of leukocytes, to thereby remove leukocytes by exclusion. In the illustrated embodiment, the media 307 also includes a prefilter material, which removes fibrin clots and other large size aggregates from the plasma.

The composition of the membrane for the media 307 can vary. For examples, hydrophilic membranes made from nylon, acrylic copolymers, polysulfone, polyvinylidene fluoride, mixed cellulose esters, and cellulose ester can be used to remove leukocytes by exclusion. Non-hydrophilic membranes can also be treated to serve as a membrane for the filter media 307. Likewise, the composition of the prefilter for the media 307 can vary. For example, the prefilter can comprise fibers of glass or polyester. Material selection takes into account customer preferences, performance objectives, and manufacturing requirements, including sterilization techniques.

In the illustrated and preferred embodiment, (see Fig. 5), the filter media 307 includes three filter media layers 342, 344, and 346. The first filter media layer 342 comprises USP Grade VI glass fiber or the equivalent. The second and third filter

media layers 344 and 346 comprise polyethersulfone (PES) membranes, which remove leukocytes by exclusion. The second and third filter media layers 344 and 346 possess pore sizes which are approximately 10 fold smaller than the size of leukocytes and which decrease in the direction of flow. The second filter media layer 344 has a pore size in the range of about 0.9 μm to about 2.0 μm, with an average pore size of about 1.2 μm. The third filter media layer 346 has a smaller pore size in the range of about 0.3 μm to about 1.5 μm, with an average pores size of about 0.8 μm. The second and third filter media layers 344 and 346 also incidently remove red blood cells by exclusion.

The filter media 307 should preferably be capable of filtering 310 ml of plasma, suspended at a head height of 3 feet, in 20 minutes.

The housing part 348A includes an inlet 350, which, in use, conveys plasma and leukocytes into contact with the prefilter layer 342. The axis 351 of the inlet 350 is generally parallel to the plane of the layer 342 to uniformly perfuse plasma across the entire prefilter layer 342.

The housing part 348B includes an outlet 352, which conveys leukocyte-reduced plasma from the second and third PES filter layers 344 and 346. As Fig. 6 shows, the interior surface of the housing part 348B is grooved, creating a fluid manifold 354 that uniformly distributes leukocyte-reduced plasma to the outlet 352.

Referring back to Fig. 1, a length of branch tubing 308 is integrally attached to the transfer tubing 304 by conventional Y-connectors 316. The branch tubing 308 forms a fluid path bypassing the filter 306. As will be described in greater detail

later, the branch tubing 308 serves to vent air.

The far end of the transfer tubing 304 carries an air pillow 310. The air pillow 310 prevents collapse of the tubing 304 and 308 caused by pressure differentials during steam sterilization of the kit 300.

The transfer tubing 304 further includes a conventional in-line frangible cannula 312 between the filter outlet 352 and the processing and storage container 302. The cannula 312 normally closes fluid the transfer tubing 304 to fluid flow.

The cannula 312 can be constructed in various ways. U.S. Patents 4,181,140 and 4,294,247 disclose representative constructions for the cannula 312, which are incorporated herein by reference. Alternatively, an external roller clamp or C-clamp of conventional construction could be used for the same purpose.

The branch tubing 308 includes a conventional in-line one-way valve 314. The valve 314 prevents fluid flow through the branch tubing 308 in the direction of the processing and storage container 302, while permitting fluid flow in the opposite direction away from the processing and storage container 302. For redundancy, the branch tubing 308 also includes an external roller clamp or C-clamp 318. The C-clamp 318 normally closes the tubing 308 between the one-way valve 314 and the processing and storage container 302.

The processing and storage container 302 can be constructed in various ways. In the illustrated and preferred embodiment, the container 302 includes an interior chamber 320. The transfer tubing 304 communicates with the chamber 320 for conveying plasma into the chamber 320. In a preferred implementation,

the chamber 320 is capable of holding between 235 to 310 mL of plasma. A normally sealed outlet port 360 also communicates with the chamber 320. The port 360 is opened when it is time to remove plasma from the chamber 320.

The chamber 320 holds a photoactive material 326. The photoactive material 326 mixes with the plasma introduced into the chamber 320. The photoactive material 320 binds to extracellular viruses that plasma introduced into the chamber 326 may carry. When exposed to light energy in a particular spectrum, the photoactive material 326 inactivates the nucleic acids of the bound viruses, rendering them nonviable.

In the illustrated and preferred embodiment, the photoactive material 326 comprises 10 mL of liquid solution containing 83 micrograms of methylene blue in water at pH 3.1, without buffers or other additives. Methylene blue, a thiazine dye, possesses the ability to bind to nucleic acids with high affinity, targeting the viruses for destruction upon exposure to a particular spectrum of light energy. Methylene blue absorbs light in the 660 nm region of the visible spectrum, which is the spectrum region where plasma is most transparent. Methylene blue inactivates a broad range of viruses, such as HIV, human hepatitis B (HBV), human hepatitis C (HCV), and Parvo virus B19, with minimal loss of therapeutic plasma proteins.

The mixture of plasma and photoactive material 326 is irradiation by light within the chamber 320 as part of a viral inactivation process. The container 302 is therefore made of a material that is substantially transparent to the applied light energy. The material for the container 302 is also adapted to withstand contemplated storage conditions

for the plasma.

In the illustrated and preferred embodiment, the applied light energy is in the white light spectrum (400 to 700 nm). The container 302 is therefore made of a plastic, poly(ethylene vinyl acetate) material. This material is transparent to white light and is also resistant to the cold temperatures at which frozen plasma is stored. This material is commercially available and is made and sold, for example, by Baxter Healthcare Corporation under the trademark PL-732® Plastic.

The container 302 also includes a flap 322, which extends below the chamber 320. The flap 322 carries a printed label 324 having identifying indicia. The flap 322 keeps the label 324 away from the chamber 320, where it could block or impede the irradiating light.

The container 302 also serves after the viral inactivation process to store the viral inactivated plasma at temperatures below - 30º C, following standard blood banking procedures.

Further details of container 302 are found in copending U.S. Patent Application, Serial No. 08/121,820, filed September 15, 1993, and entitled "Container for Irradiation of Blood Products."

As Fig. 4 shows, the kit 300 is preferably enclosed for storage and handling before use in an overwrap envelope 328 (Fig. 1 diagrammatically shows the envelope 328 in phantom lines). The overwrap envelope 328 serves multiple functions.

To minimize evaporation of the liquid photoactive material 326 from the container 302 prior to use, the envelope 328 includes a material 332 possessing a relatively low water vapor transmission rate (WVTR). In the illustrated and preferred

embodiment, the targeted WVTR is about 0.020 gh^{-1} at 25º C and 60% relative humidity.

The particular composition of the water vapor barrier material 332 can vary. In the illustrated and preferred embodiment, the water vapor barrier material 332 comprises an oriented polypropylene material having a thickness of 25 μm.

To prevent degradation of the photoactive material 326 prior to use, the envelope also includes a light filtering material 330 possessing the ability to absorb ambient light energy in the spectrum that activates the photoactive material 326. It has been discovered that, during storage and handling prior to use, the photoactive material 326 absorbs from ambient visible light (400 nm to 700 nm)the spectrum that initiates photoactivation. The incidental absorption of ambient visible light by photoactive material 326 initiates a photoreduction process, creating byproducts that are either partially or completely ineffective for viral inactivation.

For example, exposure of methylene blue to visible ambient light (whose emission spectrum includes the 660 nm region) converts the methylene blue into colorless leucomethylene blue. The leucomethylene blue photoreduction byproduct is not effective in inactivating viruses.

The particular composition of the light filtering material 330 will vary according to the light sensitivity spectrum of the particular photoactive material 326 used. In the illustrated and preferred embodiment, the light filtering material 330 comprises a blue die of phtalocyanine pigments. The blue die material 326 transmits not more than 1% of light in the range of 600 nm to 700 nm, which is the spectrum in which methylene blue is activated.

As Figs. 2 and 3 show, in the illustrated and preferred embodiment, the overwrap envelope 328 comprises sheets S1 and S2, each of which comprises a multiple layer laminate L1 and L2. The water vapor barrier material 332 constitutes one of the exterior layers of each laminated sheet S1 and S2. The blue die comprising the light filtering material 330 is printed on the interior face of the water vapor barrier material 332.

Each laminated sheet S1 and S2 also preferably includes as another exterior layer a material 334 that flows in response to heat. The presence of the material 334 makes it possible to heat seal the two sheets S1 and S2 together, forming the envelope 328.

The particular composition of the heat flowing material 334 can vary. In the illustrated and preferred embodiment, the material 334 comprises a cast polypropylene material having a thickness of about 25 μm. The heat flowing material 334 can be attached to the layer 332, for example, by a polyurethane-polyester resin-epoxy.

Laminated sheets S1 and S2 as described, with the layers 330, 332, and 334 and suited for use as the overwrap envelope 328, can be purchased from Hosokawa Yoko Co., LTD. (Japan). The sheet material from this company has a weight of 50 g/m^2 and density 1.0 g/cm^3.

The envelope 328 is created by laying the sheets S1 and S2 of the overwrap laminate together (as Fig. 3 shows) and applying pressure and heat H along the sheet edges in a heat sealing die. The pressure and heat H form a peripheral heat seal 336, which joins the sheets S1 and S2 together, forming the envelope 328 (as Fig. 4 shows).

Despite the presence of the light filtering material 330, the overwrap envelope 328 as above described nevertheless retains sufficient transparency to other visible light spectrums to allow visual inspection of the contents of the overwrap envelope 328, for quality control or customer inspection purposes.

The overwrap envelope 328, including an appropriate light filtering material 330 as just described, can be used in association with other containers or in other systems which hold liquids or other materials sensitive to ambient light degradation. For example, photoactive materials 326 activated in different spectrum regions will require accordingly different light filtering material 328. For example, 4'-(4-Amino-2-oxa)butyl-4,5'8-trimethylpsoralen (S-59) is a photoactive material usable in conjunction with platelet-containing blood suspensions. S-59 is activated by ultraviolet-A light and can undergo intramolecular reactions when exposed to ambient UV-A and short wavelength regions of visible light. To protect against such degradation of S-59 material, the light filtering material 330 can comprise a UV-A absorbent red die.

For another example, as Fig. 10 shows, instead of using a light filtering overwrap envelope 328, the kit 300 (or another system) can include an auxiliary container 362 to store the light activated material 326 before use. The walls of the container 362 include an appropriate light filtering material 330 to protect the light activated material 326 from ambient light degradation before use. In this arrangement, the photoactivated material 326 is transferred from the auxiliary container 362 to plasma before the light activation process, either before or

during filtration, or after filtration when the plasma occupies the processing and storage container 302. Of course, a container (like the container 302), which is intended to ultimately serve as a light transparent chamber, must remain free or essentially free of a light filtering material. In this arrangement, it is still desirable to provide an overwrap envelope 364 (shown diagrammatically in Fig. 10) to decrease water vapor loss of the liquid photoactive material 326 during storage and handling prior to use.

The overwrap envelope 328 (or 364 in the Fig. 10 embodiment) is torn away when it is time to use the kit 300. As Fig. 7 shows, a container 338 holding the plasma P is connected in a sterile fashion to the transfer tubing 304 near the air pillow 310. The source container 338 can, for example, hold fresh plasma or plasma that has been frozen and thawed. The plasma is harvested by conventional blood banking procedures. These procedures, which are accomplished through centrifugation of whole blood, yield plasma that is essentially free of red blood cells.

Known sterile connection mechanisms (not shown) like that shown in Spencer U.S. Patent 4,412,835 can be used for connecting the container 338 to the transfer tubing 304. These mechanisms form a molten seal between tubing ends, which, once cooled, forms a sterile weld 360. The air pillow 310 is discarded after sterile connection between the source container 338 and the transfer tubing 304 is made.

As Fig. 7 shows, once the sterile connection is made, the source container 338 is suspended above the processing and storage container 302. The operator checks to assure that the clamp 318 is closed on the bypass branch tubing 308. The operator breaks the cannula 312, and the plasma P flows by gravity head

pressure through the filter 306. The leukocyte-reduced plasma exits the filter 306 and drains into the chamber 320 of the container 302.

It has been observed that the triple layer membrane filter 306 described above provides plasma having a leukocyte level that is below the limit of flow cytometer detection (i.e., less than about one leukocyte per μL). The actual residual level of leukocytes in the plasma after filtration by the filter 306 is estimated not to exceed an average theoretical level of 0.004 leukocyte per μL. Based upon an initial leukocyte level of 0.79×10^8 per L, the leukocyte reduction percentage of the filter 306 is estimated to be about 99.99% (log reduction ≥ 4.0).

The methylene blue photoactive material 326 is mixed with the leukocyte-reduced plasma within the container 302 by manual inversion.

As Fig. 8A shows, after mixing plasma P and photoactive material 326 within the container chamber 320, the clamp 318 is opened and the container 302 squeezed. Air A is vented from the container 302, through the bypass branch tubing 308 back into the source container 338. As Fig. 8A also shows, the venting of air A also displaces residual plasma P, out of the transfer tubing 304 between the filter 306 and the container 302 and into the bypass branch tubing 308. Viruses in the residual plasma P, having never entered the container chamber 320 have not been exposed to the photoactive material 326 and therefore should be removed before undertaking the desired photoactivation process.

As Fig. 8B shows, as air venting proceeds, an amount of the mixture M of photoactive material 326 and plasma P will enter the section 305 of the transfer tubing 304 between the filter 306 and the

container 302. The mixture M is allowed to drain back into the container 302. The mixture M flushes this section of the transfer tubing 304 with the photoactive material 326 and plasma mixture. The flushing process assures that viruses still occupying this section of the tubing 304 after air venting will become mixed with the photoactive material 326. This assures that all viruses present in the container 302 and adjacent section 305 of tubing 304 are exposed to the material 326, to thereby assure the desired virucidal effect during subsequent exposure to light irradiation.

After air venting and flushing, as just described, the tubing 305 next to the container 302 is sealed closed using, for example, a dielectric tube sealer. As Fig. 9 shows, the remaining portion of the kit 300 containing the filter 306 is removed and discarded. A remnant of the tubing 305 remains connected to the container 302.

The container 302 holding the methylene blue and leukocyte-reduced plasma, and carrying a remnant of the tubing section 305, is placed into a white light chamber 356 (see Fig. 9). The chamber 356 comprises twelve fluorescent lamps 358, which supply output in the visible range (400 to 700 nm) to both sides of the container 306. The chamber 356 monitors the light intensity and adjusts exposure time to control total light dosage delivered to the container 306. The light activates the methylene blue to release singlet oxygen, which inactivates viruses in the plasma. The approximate time of illumination to deliver a targeted dose of 33 J per cm^3 is 30 minutes. Further details of the chamber 356 can be found in copending U.S. Patent Application Serial No._____, filed ____, and entitled "A System to Detect and

Identify Bags That Have Been Processed in the Illuminating Device for Inactivation of Viruses."

After the illumination step, the leukocyte-reduced plasma is frozen within the container 302 at less than -30ºC for storage using conventional blood bank practices. The plasma within the container 302 is thawed when fractionation or transfusion is required.

In the illustrated embodiment (see Fig. 1), the kit 300 includes written instructions 374 for using the kit for its intended purpose. The instructions 374 direct the technician to handle the kit in a prescribed way to best accomplish the desired therapeutic objectives, as set forth in the preceding description and shown in Figs. 7 to 9.

The instructions 374 may take various forms. Representative instructions 374 direct the technician, upon removal of the overwrap 328, to convey plasma through the tubing 304 from the source 338 through the filter 306 to separate leukocytes from the plasma. The representative instructions 374 also direct the technician to convey leukocyte-reduced plasma through the tubing 304 from the filter 306 to the transfer container 302. The representative instructions 374 also instruct the technician to mix the photoactivated material 326 with the plasma and to expose leukocyte-reduced plasma mixed with the photoactive material 326 to light that activates the photoactive material 326. The representative instructions 374 also direct the technician to store the plasma in the container 302 after the photoactivation process.

The instructions 374 can, of course, include further details based upon the particular configuration of the kit 300. For example, in the context of the kit 300 shown in Fig. 1, the

instructions 374 can direct the technician to mix the photoactivated material with leukocyte-reduced plasma within in the container chamber 320. In this context, the instructions 374 can also direct the technician to expose the container chamber 320 to light that activates the photoactive material 326 mixed within the chamber 320 with the leukocyte-reduced plasma. The instructions 374 can also direct the technician to vent air from the container chamber 320 in a path that bypasses the filter 306, which in Fig. 1 comprises the branch tubing 308. The instructions 374 can also instruct the technician to flush the tubing 304 downstream of the filter 306 with plasma and photoactive material 326 from the chamber 320.

EXAMPLE

A study was conducted to demonstrate the ability of the kit 300 when used in accordance with the instructions 374 to inactivate viruses under intended use conditions. In the study, a maximum plasma volume of 310 mL was employed to provide the lowest concentration of methylene blue and the greatest fluid thickness to be illuminated. In addition, the nominal targeted light dose of 33 J/cm^2 was reduced to 24 or 30 J/cm^2 to further stress the study conditions.

Plasma was collected from CPD anticoagulated whole blood units following routine blood bank procedures, yielding plasma that is essentially free of red blood cells. The plasma was not frozen prior to treatment during the study.

A panel of viruses was selected to represent the most significant agents that can contaminate fresh frozen plasma and to represent a broad spectrum of physical/chemical forms of viruses (i.e., lipid enveloped and non-lipid enveloped RNA and DNA viruses,

as well as intra-cellular viruses). The panel included the following viruses: BVDV (strain Singer); HIV Type 1 (HIV-1, strain III_B); human herpes simplex virus Type 1 (HSV-1, strain MacIntyre); pseudorabies virus (PRV, strain Aujeszky); simian virus Type 40 (SV-40, strain Pa-57); duck hepatitis B DHBV; and cell associated HIV (H-9/HIV, HIV III_B chronically infected H-9 cells).

These viruses were added to units of plasma before treatment in physiologically representative concentrations. A process control comprising an aliquot of virus-spiked plasma, was collected from each unit prior to processing in the kit 300. The process control served as the baseline value for the calculation of the virus load reduction, called the log reduction value (LRV). LRV represents either (i) the difference in log virus titers between the process control and the processed sample, or (ii) the difference in log virus titers between the process control and the validated sensitivity limit of the assay, if there was no recoverable virus (indicated by the use of the symbol ">" in the Table 1 below).

The virus panel and the log reduction values (LRV's) obtained by processing the plasma in the kit 300 in accordance with the instructions 374 are summarized in the following Table 1:

TABLE 1: Results of Study on Viral Inactivation Using the Kit 300

Virus	Model for	Size (nm)	LRV
HIV	Self	110	>6.6 at 24 J/cm^2
BVDV	HCV	60-70	>5.93 ± 0.07 at 24 J/cm^2
DHBV	HBV	40	3.5 at 30 J/cm^2
PRV	enveloped DNA virus	150-180	5.52 ± 0.38 at 30 J/cm^2
HSV	enveloped DNA virus	150-180	>6.16 ± 0.06 at 24 J/cm^2
SV-40	non-enveloped DNA virus	55	4.27 ± 0.30 at 24 J/cm^2
HIV/H9	virus-infected leukocytes		No Recoverable Viruses after challenge with 1x10^8 HIV/H9 cells

Table 1 demonstrates that use of the kit 300 is effective against small and large lipid enveloped viruses with either RNA or DNA genomes. Table 1 also demonstrates the capability of the kit 300 to inactivate certain non-enveloped viruses, which are not resistant to the virucidal action of methylene blue (for example, non-enveloped encephalomyocarditis virus (EMC) has demonstrated a resistance to the virucidal action of methylene blue).

The kit 300 provides more reliability and ease of use than the removal of leukocytes from plasma by lysing using conventional freeze-thaw processes. The kit 300 also provides greater removal of adventitious agents (i.e., viruses) than mere light inactivation (which does not remove intracellular agents) and/or bed-side filtering of plasma (which only removes fibrin clots, and not leukocytes).

Fig. 11 shows, as an alternative embodiment, a kit 300′ sharing many of the component parts of the kit 300 shown in Fig. 1. The common elements (which are assigned the same reference numbers as in Fig. 1) include the processing and storage container 302, the transfer tubing 304, the filter 306, the photoactive material 326, and the frangible cannula 312.

However, the kit 300′ shown in Fig. 11 does not include the branch tubing 308 and the air pillow 310.

Instead, the far end of the tubing 304 in the kit 300′ is closed by a plug 372. The kit 300′ also includes an air reservoir 370 integrally connected to the tubing 304 by the Y-connector 316 between the filter 306 and the container 302.

The air reservoir 370 takes the place of the air pillow 310. Like the pillow 310, the reservoir 370 contains a residual amount of air to prevent collapse of the tubing 304 during steam sterilization. The reservoir 370 also serves as a chamber to receive vented air and residual plasma from the container 302 at the end of the filtration process.

More particularly, using the kit 300′, plasma from the source container 338 is passed for leukocyte reduction through the filter 306 and mixed with the photoactive material 326 in the container 320 in the same manner previously described and shown in

Fig. 7.

As Fig. 12A shows, after filtration and mixing, air A is vented from the container 302 into the reservoir 370. Residual plasma P is also displaced out of the tubing section 305 and into the reservoir 370. As Fig. 12 B shows, as air venting proceeds, an amount of the mixture M of photoactive material 326 and plasma P will enter the section 305 of the transfer tubing 304 between the filter 306 and the container 302. The mixture M flushes this section of the transfer tubing 304 with the photoactive material 326 and plasma mixture.

In all other respects the process for handling the kit 300′ is the same as previously described with respect to the kit 300.

Fig. 13 shows, as another alternative embodiment, a kit 300′′ sharing many of the component parts of the kit 300 shown in Fig. 1. The common elements (which are assigned the same reference numbers as in Fig. 1) include the processing and storage container 302, the transfer tubing 304, the branch tubing 308, the filter 306, the photoactive material 326, the air pillow 310, and the frangible cannula 312. The kit 300′′ shown in Fig. 13 includes an additional in-line filter 376 in the transfer tubing 304 downstream of the filter 306. The filter 376 includes a filter media 378 that removes from plasma a second cellular species different than the species removed by the filter media 307, which second cellular species does actually or potentially entrain viral agents. In the illustrated and preferred embodiment, where the principal cellular species targeted by the filter media 307 are leukocytes, the second cellular species targeted by the second filter media 378 are platelets.

As described above in connection with the filter media 307, the pore size of the filter media 378 can be tailored to remove platelets from plasma by exclusion. It is believed that candidate materials for the media 307 formed with a pore size range of between .3μm and .45μm (which is smaller than the pore size range of the media 307) will serve to remove platelets from plasma by exclusion.

The presence of the second, downstream media 378, having a smaller pore size than the first, upstream media 307, also provides added assurance that the cellular species targeted for removal by the first media 307 (i.e., leukocytes) will, in fact, be depleted or essentially depleted from the plasma. In this respect, the smaller pore size media 378 serves both a redundant function of removing leukocytes and an added second step function of removing the smaller platelet species.

It should be appreciated that the second filter media 378 can, instead of being separately housed as the filter 378, be integrated as another layer with the already multi-layer filter media 307.

In all other respects the process for handling the kit 300'' is the same as previously described with respect to the kit 300.

Features and advantages of the invention are set forth in the following claims.

We Claim:

1. A system for treating plasma comprising

tubing adapted to be coupled to a plasma source,

a filter coupled to the tubing to separate cellular matter from the plasma conveyed from the source,

a transfer container coupled to the tubing to receive cellular matter-reduced plasma from the filter,

a source of photoactive material to be mixed with the plasma, and

the tubing including a path to vent air from the transfer container in a path that bypasses the filter.

2. A system according to claim 1

wherein the source of photoactive material is contained within the transfer container.

3. A system according to claim 1

wherein the transfer container is made, at least in part, of material that is essentially transparent to light that activates the photoactive material.

4. A system according to claim 1

and further including an overwrap enveloping the transfer container and including light filtering material that absorbs light that activates the photoactive material.

5. A system according to claim 4

wherein the overwrap includes a vapor barrier material.

6. A system according to claim 4

wherein the photoactive material comprises methylene blue, and

wherein the light filtering material

includes a blue material on the overwrap.

7. A system according to claim 6

wherein the blue material includes phtalocyanine pigments.

8. A system according to claim 1

wherein the transfer container is made of material that accommodates plasma storage.

9. A system according to claim 1

wherein the source of photoactive material comprises an auxiliary container separate from the transfer container.

10. A system according to claim 9

wherein the auxiliary container is made, at least in part, of light filtering material that absorbs light that activates the photoactive material.

11. A system according to claim 10

wherein the photoactive material comprises methylene blue, and

wherein the light filtering material includes a blue material on the auxiliary container.

12. A system according to claim 11

wherein the blue material includes phtalocyanine pigments.

13. A system according to claim 1

wherein the path vents air from the transfer container to the plasma source.

14. A system according to claim 1

wherein the path includes a one way valve that blocks fluid flow in a direction toward the transfer container while permitting fluid flow in a direction away from the transfer container.

15. A system according to claim 1

and further including an air reservoir, and

wherein the path communicates with the air reservoir.

16. A system according to claim 1 wherein the photoactive material includes methylene blue.

17. A system according to claim 1 wherein the filter removes leukocytes.

18. A system for treating plasma comprising

tubing adapted to be coupled to a plasma source,

a first filtration media coupled to the tubing to separate a first species of cellular matter from the plasma conveyed from the source,

a second filtration media coupled to the tubing in series with the first filtration media to separate a second species of cellular matter from the plasma conveyed from the source, which second species of cellular matter is essentially not removed by the first filtration media,

a transfer container coupled to the tubing to receive cellular matter-reduced plasma from the first and second filtration media, and

a source of photoactive material to be mixed with the plasma.

19. A system according to claim 18 wherein the tubing includes a path to vent air from the transfer container in a path that bypasses the first and second filtration media.

20. A system according to claim 18 wherein the source of photoactive material is contained within the transfer container.

21. A system according to claim 18 wherein the transfer container is made, at least in part, of material that is essentially transparent to light that activates the photoactive material.

22. A system according to claim 18

and further including an overwrap enveloping the transfer container and including light filtering material that absorbs light that activates the photoactive material.

23. A system according to claim 22

wherein the overwrap includes a vapor barrier material.

24. A system according to claim 22

wherein the photoactive material comprises methylene blue, and

wherein the light filtering material includes a blue material on the overwrap.

25. A system according to claim 24

wnerein the blue material includes phtalocyanine pigments.

26. A system according to claim 18

wherein the transfer container is made of material that accommodates plasma storage.

27. A system according to claim 18

wherein the source of photoactive material comprises an auxiliary container separate from the transfer container.

28. A system according to claim 27

wherein the auxiliary container is made, at least in part, of light filtering material that absorbs light that activates the photoactive material.

29. A system according to claim 28

wherein the photoactive material comprises methylene blue, and

wherein the light filtering material includes a blue material on the auxiliary container.

30. A system according to claim 29

wherein the blue material includes phtalocyanine pigments.

31. A system according to claim 18

wherein the path vents air from the transfer container to the plasma source.

32. A system according to claim 18

wherein the path includes a one way valve that blocks fluid flow in a direction toward the transfer container while permitting fluid flow in a direction away from the transfer container.

33. A system according to claim 18

and further including an air reservoir, and

wherein the path communicates with the air reservoir.

34. A system according to claim 18

wherein the photoactive material includes methylene blue.

35. A system according to claim 18

wherein the one of the first and second filtration media removes leukocytes.

36. A system according to claim 18

wherein the one of the first and second filtration media removes platelets.

37. A system according to claim 18

wherein the first filtration media removes leukocytes, and

wherein the second filtration media removes platelets.

38. A kit comprising

tubing adapted to be coupled to a blood constituent source to convey blood constituent,

a transfer container coupled to the tubing,

a source of photoactive material to be mixed with the blood constituent, and

an overwrap enveloping at least a portion of the kit and including light filtering material that absorbs light that activates the photoactive material.

39. A kit according to claim 38

wherein the photoactive material includes methylene blue.

40. A kit according to claim 39

wherein the light filtering material includes a blue material.

41. A kit according to claim 40

wherein the blue material includes phtalocyanine pigments.

42. A kit according to claim 38

wherein the photoactive material includes psoralen.

43. A kit according to claim 42

wherein the light filtering material includes a red material.

44. A kit comprising

tubing adapted to be coupled to a plasma source,

a filter coupled to the tubing to remove cellular matter from the plasma,

a transfer container coupled to the tubing to receive cellular matter-reduced plasma from the filter,

a source of photoactive material to be mixed with the plasma, and

an overwrap enveloping at least a portion of the kit and including light filtering material that absorbs light that activates the photoactive material.

45. A kit according to claim 44

wherein the photoactive material includes methylene blue.

46. A kit according to claim 45

wherein the light filtering material includes a blue material.

47. A kit according to claim 46

wherein the blue material includes

phtalocyanine pigments.

48. A kit according to claim 44

and further including instructions for using the kit following removal of the overwrap in accordance with a method comprising the steps of

conveying plasma through the tubing from the source through the filter to separate cellular matter including leukocytes from the plasma,

conveying cellular matter-reduced plasma through the tubing from the filter to the transfer container,

mixing the photoactivated material with the plasma, and

exposing leukocyte-reduced plasma mixed with the photoactive material to light that activates the photoactive material.

49. A kit comprising

tubing adapted to be coupled to a plasma source to convey plasma,

a filter coupled to the tubing to separate cellular matter from plasma conveyed from the source,

a transfer container having a chamber that holds a photoactive material, the chamber communicating with the tubing to receive cellular matter-reduced plasma from the filter, the chamber having a wall made, at least in part, from material that is essentially transparent to light that activates the photoactive material, and

an overwrap enveloping at least a portion of the kit and including material that absorbs light that activates the photoactive material.

50. A kit according to claim 49

wherein the photoactive material includes methylene blue.

51. A kit according to claim 50

wherein the light filtering material includes a blue material.

52. A kit according to claim 51

wherein the blue material includes phtalocyanine pigments.

53. A kit according to claim 49

and further including instructions for using the kit following removal of the overwrap in accordance with a method comprising the steps of

conveying plasma through the tubing from the source through the filter to separate cellular matter including leukocytes from the plasma,

conveying cellular matter-reduced plasma through the tubing from the filter to the transfer container chamber,

mixing the photoactivated material with leukocyte-reduced plasma within in the transfer container chamber, and

exposing the transfer container chamber to light that activates the photoactive material mixed within the chamber with the leukocyte-reduced plasma.

54. A kit according to claim 53

wherein the instructions include the step of storing the plasma in the transfer container chamber after the exposing step.

55. A kit comprising

tubing adapted to be coupled to a plasma source to convey plasma,

a filter coupled to the tubing to separate cellular matter from plasma conveyed from the blood source,

a transfer container coupled to the tubing to receive cellular matter-reduced plasma from the filter,

a source of liquid photoactive material to

be mixed with the plasma, and

an overwrap enveloping at least a portion of the kit and including material that both absorbs light that activates the photoactive material and reduces liquid vapor loss from the kit.

56. A kit according to claim 55

wherein the material of the overwrap includes an oriented polymer.

57. A kit according to claim 56

wherein the oriented polymer includes polypropylene.

58. A kit according to claim 55

wherein the photoactive material includes methylene blue.

59. A kit according to claim 58

wherein the light filtering material includes a blue material.

60. A kit according to claim 59

wherein the blue material includes phtalocyanine pigments.

61. A kit according to claim 55

and further including instructions for using the kit following removal of the overwrap in accordance with a method comprising the steps of

conveying plasma through the tubing from the source through the filter to separate cellular matter including leukocytes from the plasma,

conveying cellular matter-reduced plasma through the tubing from the filter to the transfer container,

mixing the photoactivated material with the plasma, and

exposing cellular matter-reduced plasma mixed with the photoactive material to light that activates the photoactive material.

62. A kit according to claim 38 or 44 or 49 or 55

wherein the overwrap envelops the entire kit.

63. A method for treating plasma carrying contaminants and at least two species of cellular matter capable of entraining contaminants, the method comprising the steps of

separating a first species of cellular matter by filtration through a first filter media, thereby removing contaminants entrained within the first species of cellular matter,

separating a second species of cellular matter by filtration through a second filter media, thereby removing contaminants entrained within the second species of cellular matter,

adding to the plasma a photoactive material, and

emitting radiation at a selected wavelength into the plasma to activate the photoactive material and thereby eradicate the contaminant that is free of entrainment by cellular matter.

64. A method for treating plasma comprising the steps of

separating from the plasma leukocytes by filtration through a first filter media,

separating from the plasma platelets by filtration through a second filter media,

adding to the plasma a photoactive material, and

emitting radiation at a selected wavelength into the plasma to activate the photoactive material.

65. A method for treating a plasma carrying contaminants and cellular matter capable of entraining

contaminants, the method comprising the steps of

conveying plasma through a first path through a filter that separates cellular matter from the plasma, thereby removing contaminants entrained within the cellular matter,

conveying the plasma from the filter through a second path that includes an attached transfer container,

mixing within the transfer container the plasma with a photoactive material to form a plasma mixture,

conveying a portion of the plasma mixture from the transfer container through a flush path that includes the second path to thereby expose contaminants in the second path to the photoactive material,

severing the second path to separate the transfer container from the filter, the transfer container, after severance from the filter, carrying a remnant of the second path, and

emitting radiation into the transfer container at a selected wavelength to activate the photoactive material in the plasma mixture and thereby eradicate the contaminant that is free of entrainment by cellular matter.

66. A method according to claim 66 wherein the flush path by passes the filter.

67. A method according to claim 66 and further including the step of venting air from the transfer container through the flush path.

68. A method according to claim 67 wherein the flush path by passes the filter.

69. A method according to claim 66 and further including the step of storing

the plasma mixture in the transfer container after the radiation emitting step.

Abstract

Systems and methods treat plasma carrying contaminants and cellular matter that are capable of entraining contaminants. The systems and methods separate cellular matter from the plasma by filtration, thereby removing contaminants entrained within the cellular matter. The system and methods add to the plasma a photoactive material. The systems and methods emit radiation at a selected wavelength into the plasma to activate the photoactive material and thereby eradicate the contaminant that is free of entrainment by cellular matter.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Robert Herman et al. — Group No. Unknown

Serial No.: Unknown — Examiner: Unknown

Filed: Herewith

For: Systems and Methods for Removing Viral Agents from Blood

Commissioner of Patents and Trademarks
Washington, D.C. 20231

SUBMISSION OF PROPOSED DRAWING AMENDMENT FOR APPROVAL BY EXAMINER (37 CFR 1.123)

Attached please find

(check applicable items)

___ a sketch in permanent ink

_X_ a copy of the original drawing(s), with red ink markings

showing proposed changes to the drawing(s) in this application for which the approval of the Examiner is requested.

Reg. No. 29,243

Tel. No. **(262) 783-1300**

____
Signature of Attorney

Daniel D. Ryan
Type or print name of Attorney
RYAN KROMHOLZ & MANION, S.C.
Post Office Box 26618
Milwaukee, Wisconsin 53226
P.O. Address

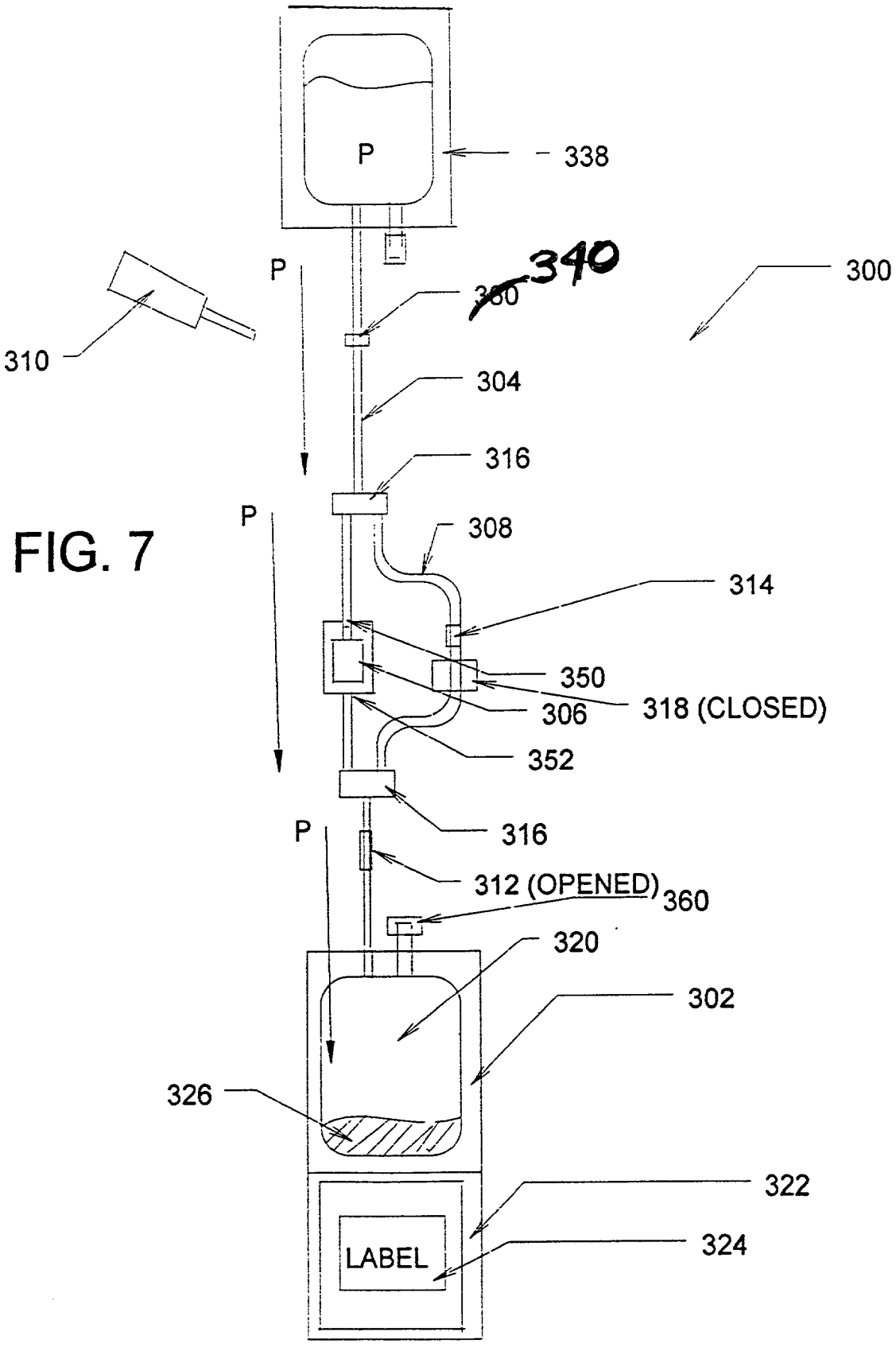
NOTE: 37 CFR 1,123 indicates that "No change in the drawing may be made except by permission of the Office" and that "A sketch in permanent ink showing proposed changes to become part of the record, must be filed for approval by the Examiner and should be a separate paper."

CERTIFICATION UNDER 37 C.F.R. 1.10*
(Express Mail label number is mandatory.)
Express Mail certification is optional.)

I hereby certify that this New Application Transmittal and the documents referred to as attached therein are being deposited with the United States Postal Service on this date 13 October 2000, in an envelope as 'Express Mail Post Office to Addressee' mailing Label Number EL574873809US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Judith Biebel
(type or print name of person mailing paper)

____
Signature of person mailing paper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306
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316
P
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302
326
322
LABEL
324

FIG. 7

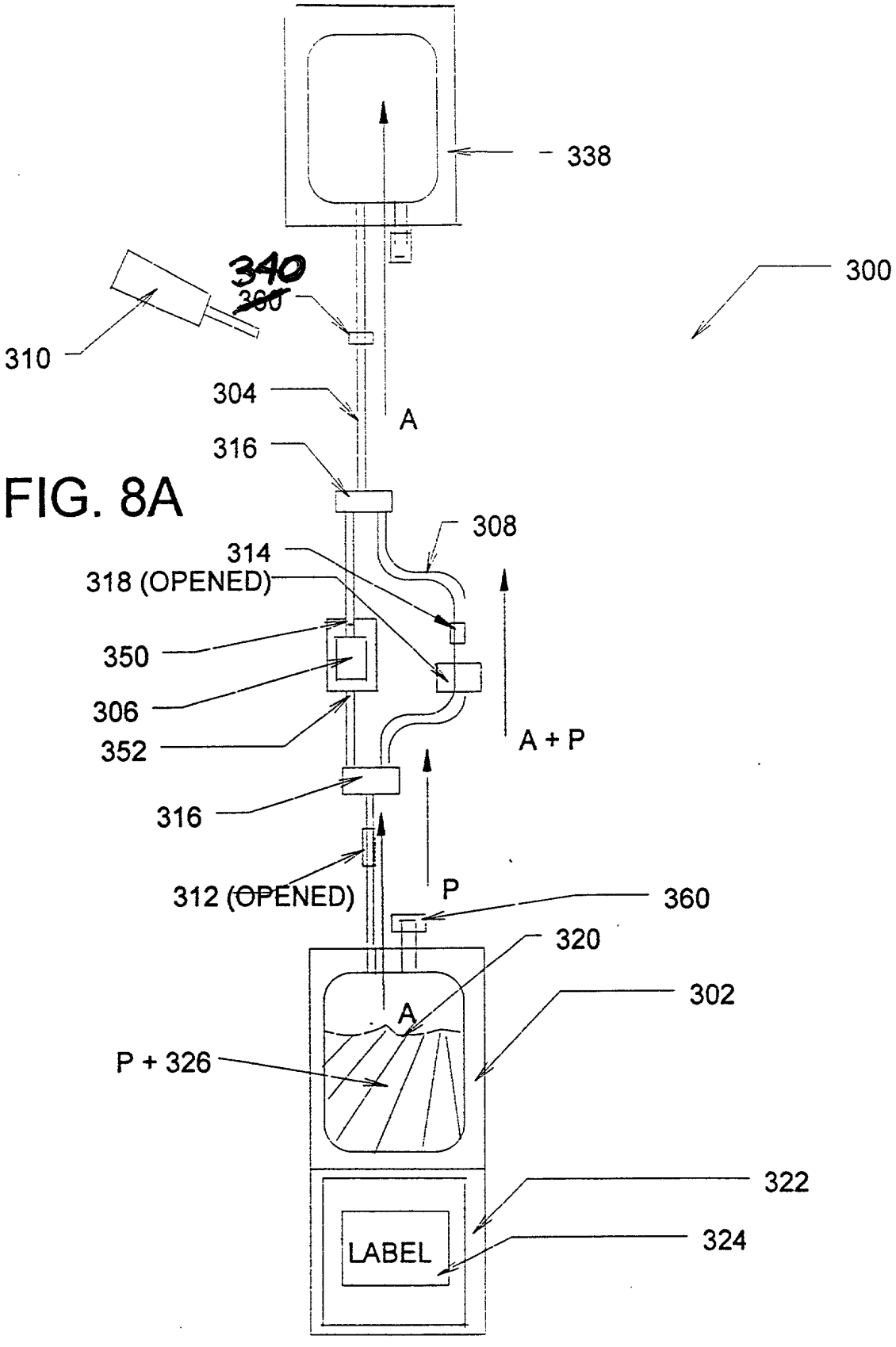
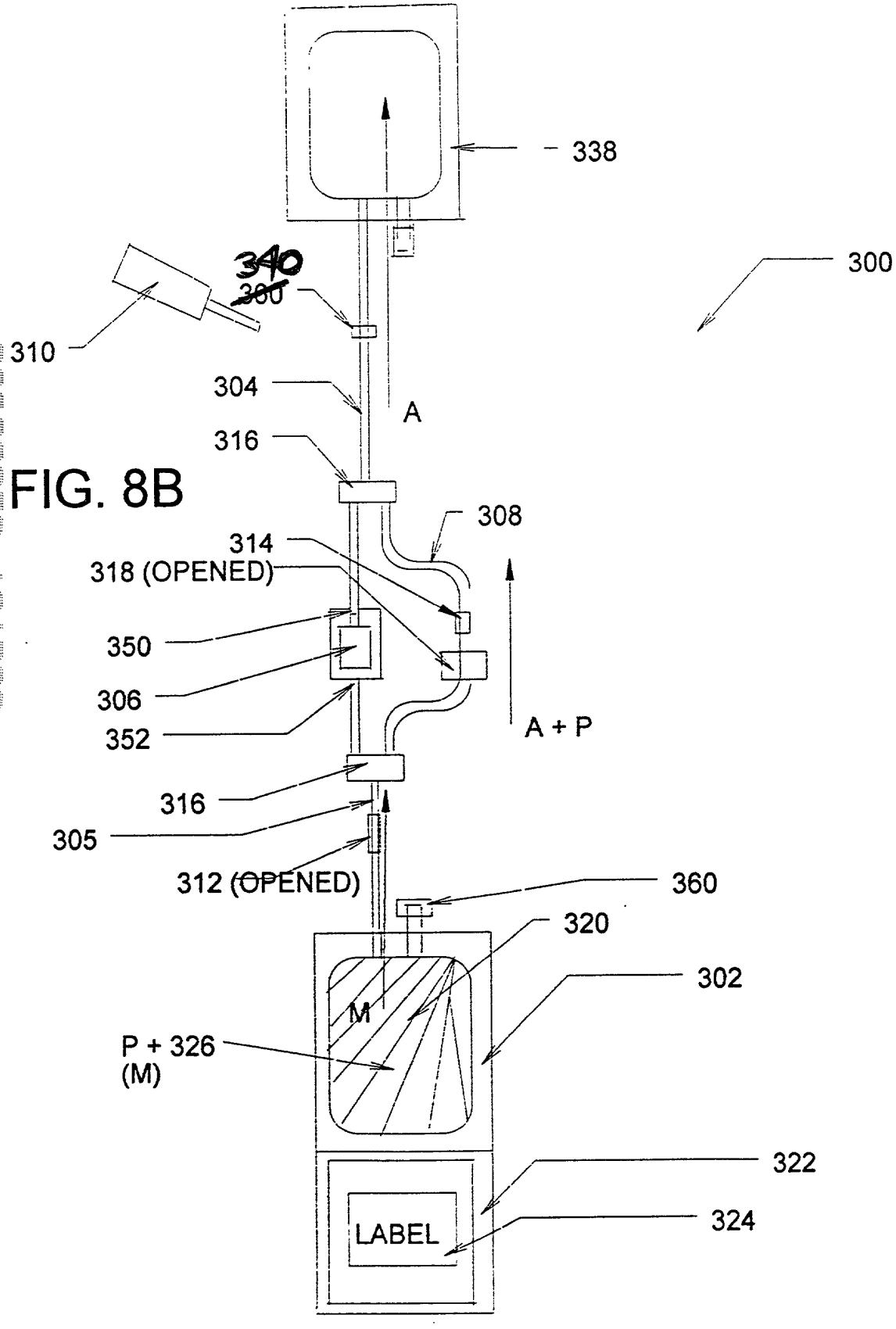


FIG. 8A


338
340
300
310
304
A
316
308
314
318 (OPENED)
350
306
352
A + P
316
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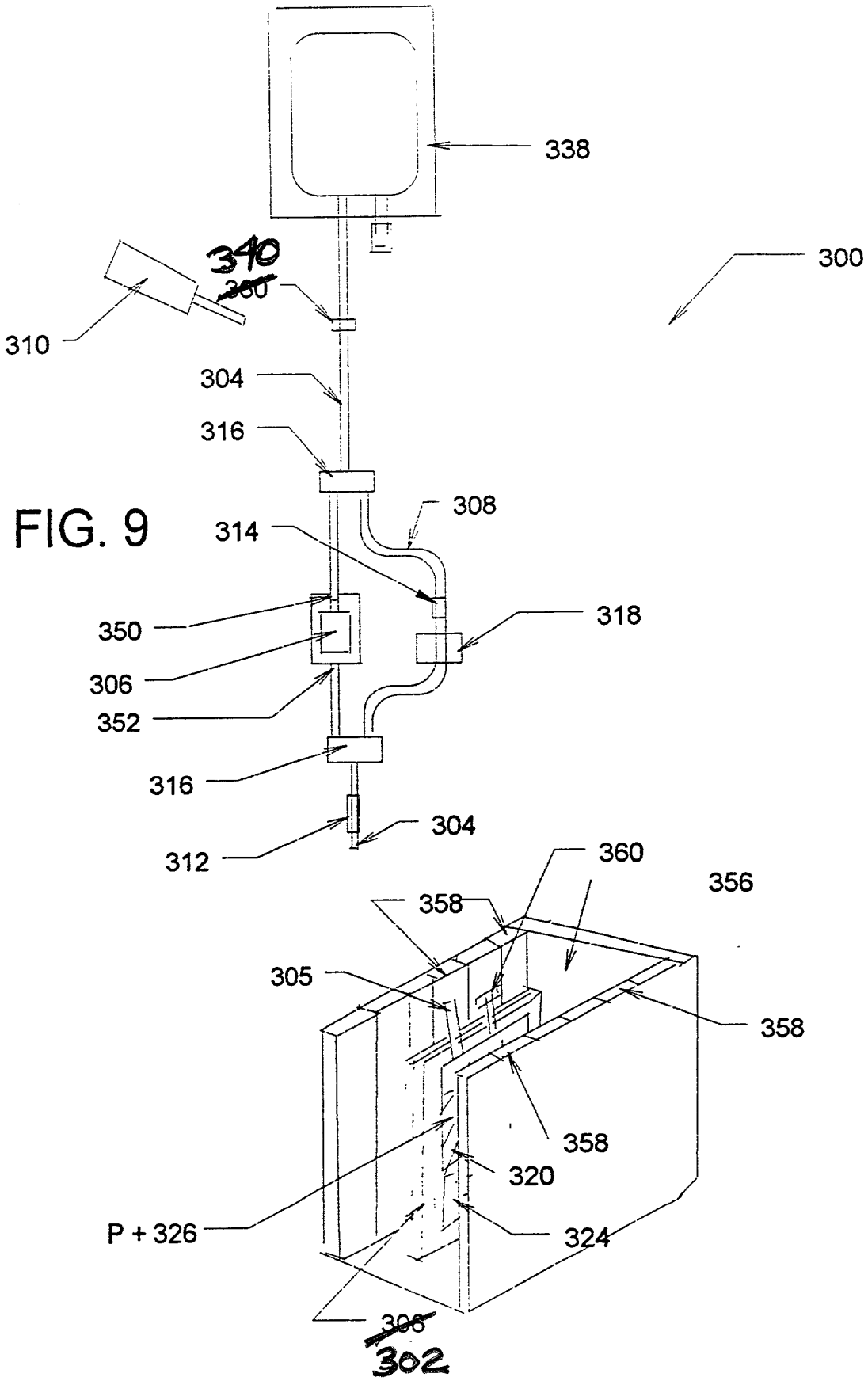
320
302
M
P + 326
(M)
322
LABEL
324

FIG. 8B

FIG. 9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308
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P + 326
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306
302

FIG. 12A

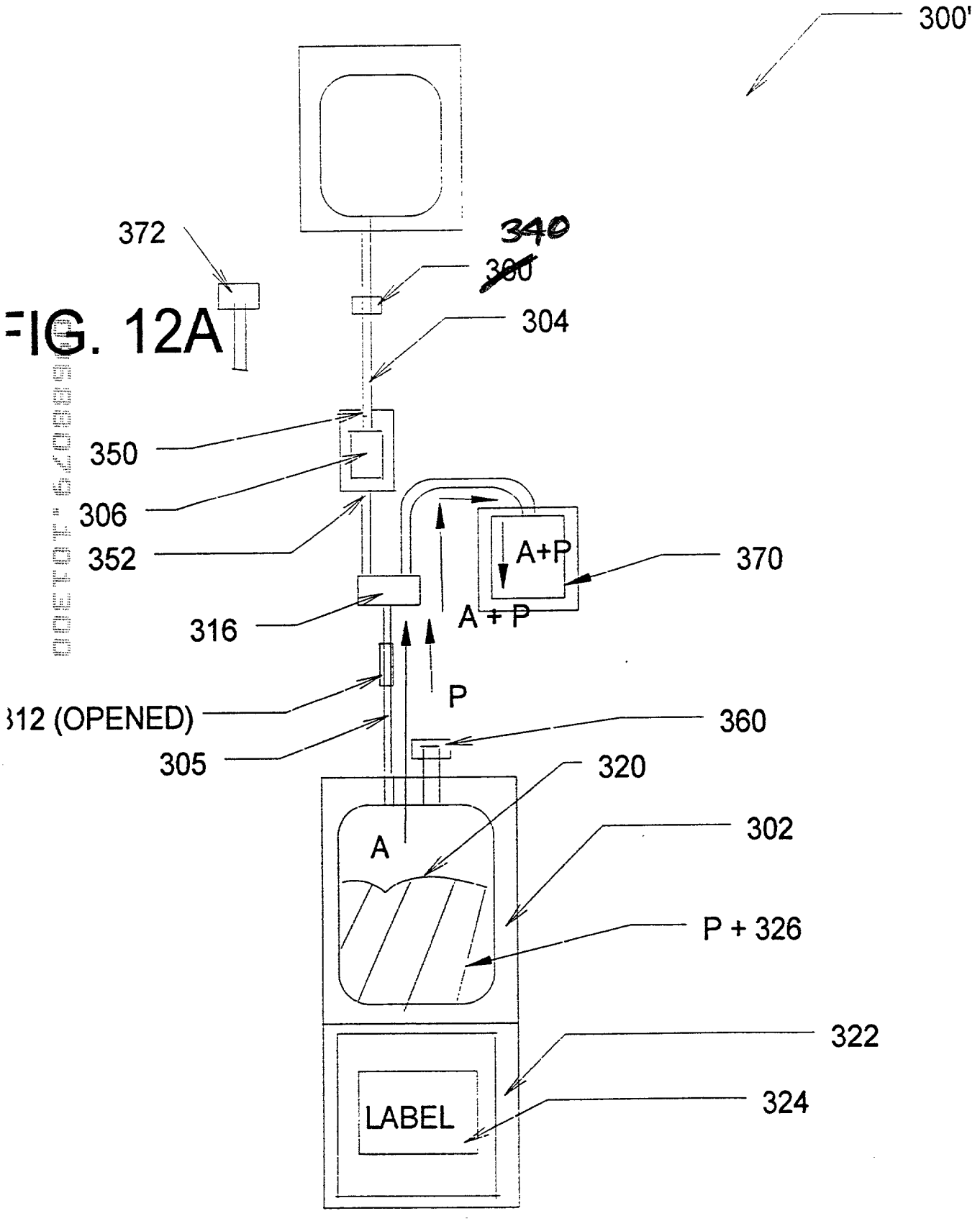
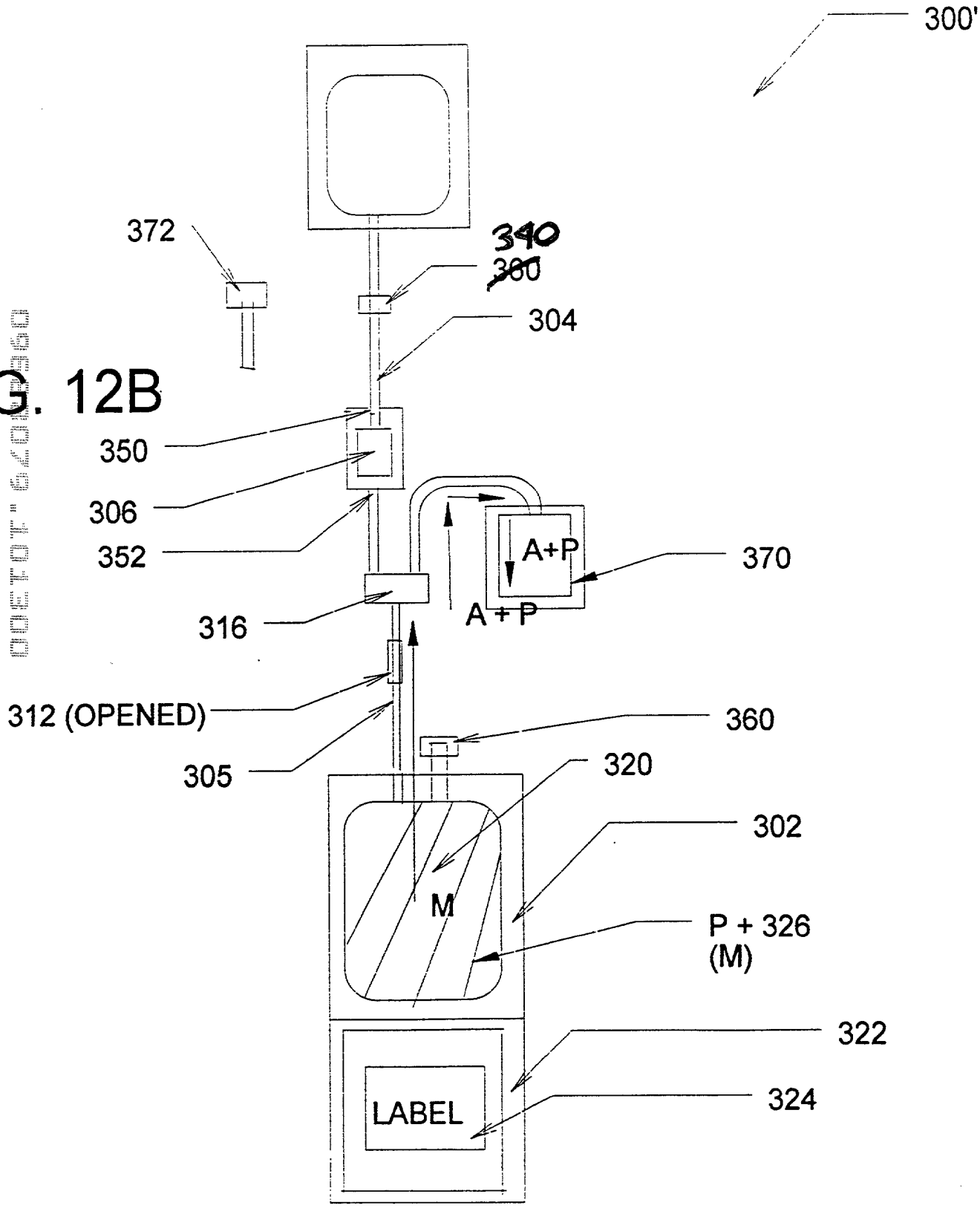

300'
372
340
360
304
350
306
352
A+P
370
316
A + P
P
312 (OPENED)
360
305
320
A
302
P + 326
322
LABEL
324

FIG. 12B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340
380
304
350
306
352
A+P
370
A + P
316
312 (OPENED)
360
305
320
302
M
P + 326
(M)
322
LABEL
324

Attorney's Docket No. F-5076

COMBINED DECLARATION AND POWER OF ATTORNEY (ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION OR CIP)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type: *(check one applicable item below)*

[x] original

[ ] design

[ ] supplemental

NOTE: If the declaration is for an International Application being filed as a divisional, continuation or continuation-in-part application do not check next item; check appropriate one of last three items.

[ ] national stage of PCT

NOTE: If one of the following 3 items apply then complete and also attach ADDED PAGES FOR DIVISIONAL, CONTINUATION OR CIP.

[ ] divisional

[ ] continuation

[ ] continuation-in-part (CIP)

INVENTORSHIP IDENTIFICATION

WARNING: If the inventors are each not the inventors of all the claims an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.

My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

Systems and Methods for Removing Viral Agents from Blood

SPECIFICATION IDENTIFICATION

the specification of which: *(complete (a), (b) or (c))*

(a) [x] is attached hereto as filed on October 28, 1996, as Serial No. 08/742,572, and the allowed claims of which are attached.

(b) [ ] was filed on _____ as [ ] Serial No. 09/_____ or [ ] Express Mail No., as Serial No. not yet known _____ and was amended on _____ (if applicable).

NOTE: Amendments filed after the original papers are deposited with the PTO which contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 CFR 1.67.

(c) [ ] was described and claimed in PCT International Application No._____ filed on and as amended under PCT Article 19 on _____ *(if any).*

ACKNOWLEDGEMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37, Code of Federal Regulations, § 1.56

(also check the following item, if desired)

[ ] In compliance with this duty there is attached an information disclosure statement in accordance with 37 CFR 1.98.

PRIORITY CLAIM (35 U.S.C. § 119)

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

(complete (d) or (e))

(d) [x] no such applications have been filed.

(e) [ ] such applications have been filed as follows.

NOTE: Where item (c) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.

A. PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. S 119

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 37 USC 119
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

_____

_____

_____

NOTE: If the application filed more than 12 months from the filing date of this application is a PCT filing forming the basis for this application entering the United States as (1) the national stage, or (2) a continuation, divisional, or continuation-in-part, then also complete ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR CIP APPLICATION for benefit of the prior U.S. or PCT application(s) under 35 U.S.C. S 120.

POWER OF ATTORNEY

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(List name and registration number)*

Daniel D. Ryan, Reg. No. 29,243
Joseph A. Kromholz, Reg. No. 34,204
John M. Manion, Reg. No. 38,957
Allan O. Maki, Reg. No. 20,623
Paul R. Puerner, Reg. No. 18,427
Arnold J. Ericsen, Reg. No. 16,879
Ralph G. Hohenfeldt, Reg. No. 17,717
Patricia Jones, Reg. No. P-46,318
Daniel R. Johnson, Reg. No. P-46,204

(check the following item, if applicable)

[ ] Attached as part of this declaration and power of attorney is the authorization of the above-named attorney(s) to accept and follow instructions from my representative(s).

SEND CORRESPONDENCE TO

Bradford R. L. Price, Esquire
Baxter Healthcare Corporation
Fenwal Division. RLP-30
P. O. Box 490
Route 120 and Wilson Road
Round Lake, Illinois 60073

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

Bradford R. L. Price
(847) 270-2632

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or first inventor

ROBERT (GIVEN NAME) E. (MIDDLE INITIAL OR NAME) HERMAN (FAMILY (OR LAST NAME))

Inventor's signature Robert E. Herman

Date 1/6/2000 Country of Citizenship USA

Residence LINDENHURST, ILLINOIS REH 1/6/2000

Post Office Address ~~542 NORTHGATE ROAD~~ 630 # GELDEN LANE

LINDENHURST, ILLINOIS

Full name of second joint inventor, if any

JOHN (GIVEN NAME) (MIDDLE INITIAL OR NAME) CHAPMAN (FAMILY (OR LAST NAME))

Inventor's signature

Date 1-3-2000 Country of Citizenship USA

Residence LAKE VILLA, ILLINOIS

Post Office Address 67 KEVIN AVENUE

LAKE VILLA, ILLINOIS 60046

Full name of third joint inventor, if any

CHONG-SON (GIVEN NAME) (MIDDLE INITIAL OR NAME) SUN (FAMILY (OR LAST NAME))

Inventor's signature

Date Country of Citizenship USA

Residence LAKE FOREST, ILLINOIS

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Full name of fourth joint inventor, if any

JEAN (GIVEN NAME) M. (MIDDLE INITIAL OR NAME) MATHIAS (FAMILY (OR LAST NAME))

Inventor's signature

Date Country of Citizenship BELGIUM

Residence LILLOIS, BELGIUM

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Full name of fifth joint inventor, if any

VERONIQUE (GIVEN NAME) (MIDDLE INITIAL OR NAME) MAYAUDON (FAMILY (OR LAST NAME))

Inventor's signature

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Residence ESTINNES, BELGIUM

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SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or first inventor

ROBERT	E.	HERMAN
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Inventor's signature _____

Date _____ Country of Citizenship USA

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Full name of second joint inventor, if any

JOHN		CHAPMAN
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Inventor's signature _____

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Residence LAKE VILLA, ILLINOIS

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Full name of third joint inventor, if any

CHONG-SON		SUN
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Full name of fourth joint inventor, if any

JEAN	M.	MATHIAS
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Full name of fifth joint inventor, if any

VERONIQUE		MAYAUDON
(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

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Full name of sole or first inventor

ROBERT	E.	HERMAN
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Inventor's signature _____
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Full name of second joint inventor, if any

JOHN		CHAPMAN
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Full name of third joint inventor, if any

CHONG-SON		SUN
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Full name of fourth joint inventor, if any

JEAN	M.	MATHIAS
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Full name of fifth joint inventor, if any

VERONIQUE		MAYAUDON
(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

Inventor's signature _____
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Full name of sole or first inventor

ROBERT (GIVEN NAME) _____ E. (MIDDLE INITIAL OR NAME) HERMAN (FAMILY (OR LAST NAME)

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JOHN (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) CHAPMAN (FAMILY (OR LAST NAME)

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CHONG-SON (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) SUN (FAMILY (OR LAST NAME)

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Full name of fourth joint inventor, if any

JEAN (GIVEN NAME) M. (MIDDLE INITIAL OR NAME) MATHIAS (FAMILY (OR LAST NAME)

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Full name of fifth joint inventor, if any

VERONIQUE (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) MAYAUDON (FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship BELGIUM

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Full name of sole or first inventor

ROBERT (GIVEN NAME) _____ E. (MIDDLE INITIAL OR NAME) HERMAN (FAMILY (OR LAST NAME)

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Full name of second joint inventor, if any

JOHN (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) CHAPMAN (FAMILY (OR LAST NAME)

Inventor's signature _____

Date 1-3-2000 Country of Citizenship USA

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Full name of third joint inventor, if any

CHONG-SON (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) SUN (FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship USA

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Full name of fourth joint inventor, if any

JEAN (GIVEN NAME) M. (MIDDLE INITIAL OR NAME) MATHIAS (FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship BELGIUM

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Full name of fifth joint inventor, if any

VERONIQUE (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) 7 Jan 2000 MAYAUDON (FAMILY (OR LAST NAME)

Inventor's signature _____

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~~7120 ESTINNES, BELGIUM~~ 59600 GOGNIES-CHAUSSEE
VM 7-1-00 FRANCE

CHECK PROPER BOX FOR ANY OF THE FOLLOWING ADDE GE(S) WHICH FORM A PART OF THIS DECLARATION

[ ] Signature for sixth and subsequent joint inventors. Number of pages added 1

* * *

[ ] Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. Number of pages added __________

* * *

[ ] Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 CFR 1.47. Number of pages added ________

* * *

[ ] Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (CIP) application.

[ ] Number of pages added __________

* * *

[ ] Authorization of attorney(s) to accept and follow instructions from representative

* * *

(If no further pages form a part of this declaration then end this declaration with this page and check the following item:)

[ ] This declaration ends with this page

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or sixth inventor

SERGE (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) de GHELDERE (FAMILY (OR LAST NAME)

Inventor's signature Serge de Ghelderes

Date 13 JAN 2000 Country of Citizenship BELGIUM

Residence HOEILAART, BELGIUM

Post Office Address WAVERSESTEENWEG 101

HOEILAART – 1560, BELGIUM

Full name of seventh joint inventor, if any

DANIEL (GIVEN NAME) J. (MIDDLE INITIAL OR NAME) BISCHOF (FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship USA

Residence McHENRY, ILLINOIS

Post Office Address 4913 RAINTREE COURT

McHENRY, ILLINOIS 60050

Full name of eighth joint inventor, if any

_____ (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) _____ (FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or sixth inventor

SERGE		de GHELDERE
(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship BELGIUM

Residence HOEILAART, BELGIUM

Post Office Address WAVERSESTEENWEG 101

HOEILAART – 1560, BELGIUM

Full name of seventh joint inventor, if any

DANIEL	S. F.	BISCHOF
(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

Inventor's signature Daniel F. Bisch DF 1/6/00

Date 1/6/00 Country of Citizenship USA

Residence McHENRY, ILLINOIS

Post Office Address 4913 RAINTREE COURT

McHENRY, ILLINOIS 60050

Full name of eighth joint inventor, if any

(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

PATENT

Attorney's Docket No. F-5076

COMBINED DECLARATION AND POWER OF ATTORNEY (ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION OR CIP)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type: *(check one applicable item below)*

[x] original

[ ] design

[ ] supplemental

NOTE: If the declaration is for an International Application being filed as a divisional, continuation or continuation-in-part application do not check next item; check appropriate one of last three items.

[ ] national stage of PCT

NOTE: If one of the following 3 items apply then complete and also attach ADDED PAGES FOR DIVISIONAL, CONTINUATION OR CIP.

[ ] divisional

[ ] continuation

[ ] continuation-in-part (CIP)

INVENTORSHIP IDENTIFICATION

WARNING: If the inventors are each not the inventors of all the claims an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.

My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

Systems and Methods for Removing Viral Agents from Blood

SPECIFICATION IDENTIFICATION

the specification of which: *(complete (a), (b) or (c))*

(a) [ ] is attached hereto.

(b) [x] was filed on October 28, 1996 as [x] Serial No. 08/ 742,572 or [ ] Express Mail No., as Serial No. not yet known _____ and was amended on _____(if applicable).

NOTE: Amendments filed after the original papers are deposited with the PTO which contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 CFR 1.67.

(c) [ ] was described and claimed in PCT International Application No._____ filed on and as amended under PCT Article 19 on _____ *(if any).*

ACKNOWLEDGEMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37, Code of Federal Regulations, § 1.56

(also check the following item, if desired)

[ ] In compliance with this duty there is attached an information disclosure statement in accordance with 37 CFR 1.98.

PRIORITY CLAIM (35 U.S.C. § 119)

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

(complete (d) or (e))

(d) [x] no such applications have been filed.

(e) [ ] such applications have been filed as follows.

NOTE: Where item (c) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.

A. PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. S 119

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 37 USC 119
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

NOTE: If the application filed more than 12 months from the filing date of this application is a PCT filing forming the basis for this application entering the United States as (1) the national stage, or (2) a continuation, divisional, or continuation-in-part, then also complete ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR CIP APPLICATION for benefit of the prior U.S. or PCT application(s) under 35 U.S.C. S 120.

POWER OF ATTORNEY

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(List name and registration number)*

Ralph G. Hohenfeldt (17,717)
Daniel D. Ryan (29,243)
Allan O. Maki (20,623)
Philip P. Mann (30,960)

(check the following item, if applicable)

[ ] Attached as part of this declaration and power of attorney is the authorization of the above-named attorney(s) to accept and follow instructions from my representative(s).

SEND CORRESPONDENCE TO

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DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

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(847) 270 - 2632

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or first inventor

ROBERT (GIVEN NAME) E. (MIDDLE INITIAL OR NAME) HERMAN (FAMILY (OR LAST NAME))

Inventor's signature X Robert E. Herman

Date X June 9, 1997 Country of Citizenship

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Full name of second joint inventor, if any

JOHN (GIVEN NAME) (MIDDLE INITIAL OR NAME) CHAPMAN (FAMILY (OR LAST NAME))

Inventor's signature X John Chapman

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CHONG-SON (GIVEN NAME) (MIDDLE INITIAL OR NAME) SUN (FAMILY (OR LAST NAME))

Inventor's signature X Chong-Son Sun

Date X 6/10/97 Country of Citizenship

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Full name of fourth joint inventor, if any

JEAN (GIVEN NAME) M (MIDDLE INITIAL OR NAME) MATHIAS (FAMILY (OR LAST NAME))

Inventor's signature

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Full name of fifth joint inventor, if any

VERONIQUE (GIVEN NAME) (MIDDLE INITIAL OR NAME) MAYAUDON (FAMILY (OR LAST NAME))

Inventor's signature

Date Country of Citizenship BELGIUM

Residence ESTINNES, BELGIUM

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SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or first inventor

ROBERT		HERMAN
(GIVEN NAME)	(MIDDLE INITIAL OR NAME)	FAMILY (OR LAST NAME)

Inventor's signature ______
Date ______ Country of Citizenship ______
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Post Office Address ______

Full name of second joint inventor, if any

JOHN		CHAPMAN
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Inventor's signature ______
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Full name of third joint inventor, if any

CHONG	S	SUN
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Full name of fourth joint inventor, if any

JEAN	M	MATHIAS
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Inventor's signature X [signature]
Date X 13 MAY 1997 Country of Citizenship BELGIUM
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Full name of fifth joint inventor, if any

VERONIQUE		MAYAUDON
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Inventor's signature ______
Date ______ Country of Citizenship FRANCE
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SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sole or first inventor

ROBERT (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) HERMAN (FAMILY (OR LAST NAME))

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

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Full name of second joint inventor, if any

JOHN (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) CHAPMAN (FAMILY (OR LAST NAME))

Inventor's signature _____

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Residence LAKE VILLA, ILLINOIS

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[redacted]

Full name of third joint inventor, if any

CHONG (GIVEN NAME) S (MIDDLE INITIAL OR NAME) SUN (FAMILY (OR LAST NAME))

Inventor's signature _____

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Full name of fourth joint inventor, if any

JEAN (GIVEN NAME) M (MIDDLE INITIAL OR NAME) MATHIAS (FAMILY (OR LAST NAME))

Inventor's signature _____

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Full name of fifth joint inventor, if any

VERONIQUE (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) MAYAUDON (FAMILY (OR LAST NAME))

Inventor's signature X _____

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CHECK PROPER BOX(ES) FOR ANY OF THE FOLLOWING ADDED PAGE(S) WHICH FORM A PART OF THIS DECLARATION

[x] Signature for sixth and subsequent joint inventors. Number of pages added 1

* * *

[ ] Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. Number of pages added _____

* * *

[ ] Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 CFR 1.47. Number of pages added _____

* * *

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* * *

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* * *

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NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sixth joint inventor, if any

SERGE (GIVEN NAME) | (MIDDLE INITIAL OR NAME) | de GHELDERE (FAMILY (OR LAST NAME))

Inventor's signature X

Date X 24 April '97 Country of Citizenship BELGIUM

Residence HOEILAART, BELGIUM

Post Office Address WAVERSESTEENWEG 101

HOEILAART - 1560, BELGIUM

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Full name of seventh joint inventor, if any

DANIEL (GIVEN NAME) | J (MIDDLE INITIAL OR NAME) | BISCHOF (FAMILY (OR LAST NAME))

Inventor's signature

Date Country of Citizenship USA

Residence McHENRY, ILLINOIS

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Full name of eighth joint inventor, if any

(GIVEN NAME) | (MIDDLE INITIAL OR NAME) | (FAMILY (OR LAST NAME))

Inventor's signature

Date Country of Citizenship

Residence

Post Office Address

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name as it should appear on the filing receipt and all other documents.

Full name of sixth joint inventor, if any

SERGE (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) de Gheldere (FAMILY (OR LAST NAME))

Inventor's signature Serge de Gheldere

Date _____ Country of Citizenship BELGIUM

Residence _____ Waversesteenweg 101

Post Office Address _____ HOEILAART - 1560

_____ BELGIUM

Full name of seventh joint inventor, if any

DANIEL (GIVEN NAME) F. (MIDDLE INITIAL OR NAME) BISCHOF (FAMILY (OR LAST NAME))

Inventor's signature X

Date X 6/13/97 Country of Citizenship USA

Residence McHENRY, ILLINOIS

Post Office Address 4913 RAINTREE COURT

McHENRY, ILLINOIS 60050

[redacted]

Full name of eighth joint inventor, if any

_____ (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) _____ (FAMILY (OR LAST NAME))

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

_____

PATENT

Attorney Docket No. F-5076 DIV

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Herman et al. Group No.: Unknown

Serial No.: Unknown Examiner: Unknown

Filed: Herewith

For: Systems and Methods for Removing Viral Agents from Blood

Assistant Commissioner for Patents
Washington, D.C. 20231

ASSOCIATE POWER OF ATTORNEY (37 CFR 1.34)

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NOTE: Correspondence will be had with the associate attorney, unless the principal attorney directs otherwise. MPEP § 403.01.

NOTE: An associate attorney may not appoint another attorney. MPEP § 402.02.

(Signature of Principal Attorney of Record)

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